UNIVERSITY OF BIRMINGHAM

FACULTY OF MEDICINE

WILLIAM WITHERING MEMORIAL LECTURESHIP

ORGANIC INHERITANCE IN MAN

TABLE 3.—

Michelia fu
Myrica pen
Olea europa
Pernettya m
Picea abies

Picea maria
Pinus densi
Populus sp
Prunus cera
Prunus nan
Prunus sub

Quercus rob
Quercus sub
Rhamnus f
Rhododendr
**Rhododend*

Rhododendr

**Rhododend*
Rhododendr

**Rhododend*
Rhododendr
**Rhododend*

Rosa canin
Rosa multi

Rosa willm
Rubus delic
Syringa am
Tamarix g
Thea sp. . .
Thuja orie
Vangueria
Vibu
Vib
**V*
Vi

ORGANIC INHERITANCE IN MAN

BY

F. A. E. CREW, M.D., D.Sc., Ph.D.

DIRECTOR OF THE ANIMAL BREEDING RESEARCH DEPARTMENT,
THE UNIVERSITY, EDINBURGH

OLIVER AND BOYD
LONDON: 33 PATERNOSTER ROW, E.C.
EDINBURGH: TWEEDDALE COURT
1927

TABLE 3.—

Michelia fu
Myrica per
Olea europ
Pernettya m
Picea abies

Picea mari
Pinus dens
Populus sp
Prunus cer
Prunus nan
Prunus sub

Quercus rob
Quercus su
Rhamnus f
Rhododend
**Rhododen*

Rhododend

**Rhododen*
Rhododend

**Rhododen*
Rhododend
**Rhododen*

Rosa canin
Rosa multi

Rosa willm
Rubus delic
Syringa am
Tamarix g
Thea sp. . .
Thuja orie
Vangueria
Viburnum
Vib n
**V*
Vi

PRINTED IN GREAT BRITAIN BY
OLIVER AND BOYD, EDINBURGH

TO

MY SON AND MY DAUGHTER

WHO I HOPE HAVE RECEIVED BY WAY
OF ME THOSE QUALITIES WHICH, IN
MY PARENTS, I FIND SO ADMIRABLE

TABLE 3.-

Michelia f
Myrica pe
Olea europ
Pernettya
Picea abies

Picea mari
Pinus dens
Populus sp
Prunus cer
Prunus na
Prunus sub

Quercus rob
Quercus sub
Rhamnus f
Rhododendr
**Rhododend*

Rhododendr

**Rhododend*
Rhododendr

**Rhododend*
Rhododendr
**Rhododend*

Rosa canina
Rosa multif

Rosa willmo
Rubus delic
Syringa am
Tamarix ga
Thea sp. . .
Thuja orien
Vang
Vibu
Vib
**Vi*
Vit

PREFACE

THIS book embodies the subject-matter of the course of lectures given in 1927 in Birmingham University by the author as the first William Withering Memorial lecturer.

The lectures were addressed to members of the medical profession, particularly to the general practitioner. This being so, it seems reasonable, now that the lectures are to be published, to avoid any strenuous effort to observe meticulous accuracy and elaborate detail, but rather to attempt to give an intelligible presentation of principle. Authorities, though abundantly quoted, are not named, and there is no bibliography: such references as cannot be found in *Menschliche Erblichkeitslehre* (Baur, Fischer, Lenz), or *Heredity and Eugenics* (Gates), can be obtained, if desired by any reader of this book, from the author.

F. A. E. C.

EDINBURGH, *September* 1927.

WILLIAM WITHERING

WILLIAM WITHERING, M.D., F.R.S.

[This account of the life of William Withering and the reproduction of his portrait are taken from the *Birmingham Medical Review*, vol. i., no. 1, 1926, and I am indebted to the Editor and publishers for this privilege, and to Professor W. H. Wynn for permission to quote largely and verbatim from his memoir.]

ON the long roll of physicians to the General Hospital, Birmingham, the name of William Withering stands pre-eminent. Known to fame as having introduced digitalis into medical treatment, he was the most distinguished provincial physician of his day, a philosopher and friend of philosophers, and a botanist of European repute, with almost as great a reputation as a mineralogist and chemist.

He was descended from an old Shropshire family. His father had an extensive medical practice in the county, and his mother was the sister of Dr Brooke Hector, of Lichfield. He was born at Wellington, 17th March 1741, and was educated at home, having as a tutor in classical subjects the Rev. Henry Wood, of Ercall, a considerable scholar, to whom his pupil always felt a deep sense of obligation. The example of his father and uncles naturally turned his thoughts to the medical profession, and in 1762 he matriculated at Edinburgh University and commenced the study of anatomy and chemistry. He quickly made friends, became a Freemason, and was elected to the Medical Society. As a student he was very industrious, and spent his evenings in transcribing his lectures notes, many written folios and quartos, illustrated by neat drawings, testifying to his diligence. His "Adversaria," we are told by his son,

contained nearly a thousand pages, alphabetically arranged according to subjects. This burning of the midnight oil affected his health and, as a corrective, he took up golf. He was fond of music, and excelled on the German flute and harpsichord. He attempted the lighter kinds of poetry and, under a pseudonym, published several pieces in periodicals. He became a connoisseur of painting and invented an instrument to facilitate drawing in perspective. In spite of these pursuits he had time to form a society, the "Sodalitium Romanum," which met weekly for the purpose of acquiring a facility in speaking Latin. He took an active part in the meetings of the Medical Society, and early in 1764 read his first paper on "Topical Blood-letting," and soon afterwards published a treatise on "Inflammation of the Pericardium," which received the praise and support of Professor Cullen. He communicated a Latin commentary on an "Aphorism of Hippocrates," forbidding sudden changes in diet and exercise, and wrote a dissertation on "Dropsy." These were followed by a treatise on "The Causes, Diagnosis, and Cure of Rickets," a practical history of "Angina Inflammatoria," and another "Aphorism."

The year 1765 was mainly spent in attendance at various London hospitals, but in 1766 he returned to Edinburgh, and was so anxious to excel that he spared no time for recreation. He offered for his thesis for graduation, "Malignant Putrid Sore Throat." This was later expanded into a treatise which, in gratitude to his early instructors, is dedicated to Dr Brooke Hector and Rev. Henry Wood. Having passed his examination with credit, he obtained the degree of Doctor of Physic on 31st July 1766. After a visit to London and Oxford he decided to visit Paris, then famous for its surgery. An additional inducement was an invitation from the Surgeon-in-Ordinary to the King of France, whom he had met in London. His visit was marred by the unfortunate illness and death of his travelling companion, Mr Townsend. A commissaire placed the seals

of office upon the effects of his dead friend with the intention of confiscating them as belonging to a foreigner dying in the profession of the reformed religion. Withering, in no wise deterred by menaces, insisted upon the property being restored, and with the aid of the British Ambassador this was done. This unpleasant experience filled his mind with disgust of arbitrary power, and did much to kindle the love of liberty which afterwards marked his political opinions. He apparently did not profit much by his visit, and considered the practice of French physicians less judicious than that in England.

It was now necessary for him to decide where to settle down. From Chester and Coventry he received flattering invitations, but the death of Dr Buchanan caused a vacancy at Stafford, of which he at once availed himself. Here he soon enjoyed the best society of the county, his musical talent making him a welcome guest. He took part in amateur theatricals, and we read of him in 1769 visiting Stratford-on-Avon for the Shakespeare Jubilee, held that year under the direction of David Garrick. One of Withering's earliest patients was the lady who became his wife. After establishing her health, he was permitted, in some degree, to direct the completion of her education. "The harpsichord, the voice, the pencil, and every exterior accomplishment," he quaintly observes, "were already at her command, my study was to extend her taste for literature." It is suggested that his first researches in the British flora were induced by his desire of supplying subjects for the drawings of this lady. About this time he contrived a microscope, more portable and convenient than any previously constructed.

In 1766 the Stafford Infirmary had been built, and Withering was the sole physician. There still exists in the Infirmary a Withering Samaritan Fund for sending poor patients after serious illness or operations to convalescent homes. On 12th September 1772, he married Helena

Cooke, and his new responsibility made him reconsider his prospects. His professional income for the last six years had scarcely produced one hundred pounds per annum, and no one will accuse him of an unreasonable ambition in seeking a wider field for his talents. In 1775 the opportunity arrived, and he left Stafford for Birmingham, but his interest in the Infirmary was so keen that he performed a weekly journey of nearly sixty miles to see patients there until a successor could be found. The removal to Birmingham fully answered expectations, and during the first twelve months his professional income more than doubled that of his best year in Stafford, and in a short time, notwithstanding his attention to chemistry and botany, his income reached £1000. His friendship with Matthew Boulton, then the outstanding figure in Birmingham, doubtless had much to do with his success.

In the summer of 1776 he published *A Botanical Arrangement of all the Vegetables growing in Great Britain, according to the system of the celebrated Linneus: with an Easy Introduction to the Study of Botany*, in two volumes; and no sooner had he completed this considerable work than he translated Bergman's essay, *De Analysi Aquarum*. As an exercise in analysis, he proved the contents of St Erasmus's Well and the Salt Marsh Water near Ingestre, Rowton Well in Sutton Park, and several other springs. He also compounded in exact imitation the waters of Spa, Pyrmont and Seltzer. His pursuits varied with the season. In the winter he wrote, "Botany now no longer presides at my board—her season is past, and chymistry overspreads the table. I have completely succeeded in the analysis of the Nevil Holt water, which I can destroy and reproduce at pleasure. It cost me much labour, but has well repaid my attention by the production of a salt not hitherto supposed to exist in the earth, which I call Muria Aluminosa. It is formed of marine acid and earth of alum." These results were intended for the Royal Society. Experiments on the

solubility of saline substances, on Peruvian bark, on human calculi, and other physiological researches, followed in quick succession, whilst he was also engaged in the construction of philosophical apparatus, especially on the improvement of electrical machines. He assisted Baron Dillon by adding chemical and botanical notes to his *Travels through Spain*. His scientific notoriety led to much correspondence, and specimens were constantly being brought to him for examination.

His hard work, however, interfered with his health, and in 1776 he had an attack of irregular fever, which was the first indication of the tuberculosis which later frankly declared itself. It was a prelude to further attacks, and the winter seasons always deprived him of his usual energy.

In 1779 he was appointed one of the first four physicians to the General Hospital, the erection of which was begun in 1766, but had been suspended for twelve years owing to lack of funds.

In 1778 a severe epidemic of scarlet fever visited Birmingham, and an account of the disease was published by Withering in a book entitled *An Account of the Scarlet Fever and Sore Throat or Scarlatina Anginosa, particularly as it Appeared in Birmingham in the Year* 1778. At first Withering thought that scarlatina anginosa and angina gangrenosa or ulcerated sore throat were two distinct diseases, but in the second edition of this work, published in 1793, he had become persuaded that they were varieties of one disease. He gives a graphic description of scarlet fever and the dropsy which often followed. He was convinced of its contagiousness, and put down the incubation period at three or four days. He opposed bleeding and purgatives in treatment, but advocated the use of emetics, as following nature's method of getting rid of the poison, and antiseptics to the throat. His remarks on isolation are wise, and he points out the futility of closing schools or sending healthy families away from infected families. It

seems probable from the descriptions of angina gangrenosa that the term included cases of Vincent's angina and that Withering was right in his first opinion that this was a separate disease from scarlatina anginosa.

In 1782 we find him much engaged upon chemical investigations, especially the analysis of various earths, and he published papers on "An Analysis of Two Mineral Substances," viz., the Rowley Ragstone and the Toadstone, and "Experiments on Different Kinds of Marl found in Staffordshire." He was much interested in the "Phlogiston Theory," then a subject of controversy, and read some humorous verses to the Lunar Society, entitled "The Life and Death of Phlogiston." Had he prosecuted this line of investigation, it seems probable that he would have anticipated Lavoisier in the final overthrow of the Phlogiston Theory.

In the spring of 1783, a return of his lung trouble compelled him to rest for a few months, but later in the year he translated Bergman's *Sciagraphia Regni Mineralis* under the title of *Outlines of Mineralogy*, and also communicated to the Royal Society "Experiments and Observations on the Terra Ponderosa." This mineral, barium carbonate, was afterwards named Witherite in his honour. In this year he met the celebrated Quaker lady Mrs Knowles, the heroine of several well-known passages in Boswell's *Life of Johnson*, and with her he conducted a lively correspondence for several years. During 1784 he spent several months at Boulton's house in Soho, then a rural retreat, and by this means he so restored his health that he began the preparation of a second edition of his botanical work. This was soon interrupted by reports of the misuse of his method of giving foxglove for dropsy, and also of claims of priority by some to whom he had taught his methods. He was thus forced to publish sooner than he intended, and in 1785 appeared *An Account of the Foxglove, and some of its Medical Uses: with practical remarks on Dropsy and other Diseases.*

In 1775 his opinion had been asked concerning a family recipe for dropsy which was the secret of an old woman in Shropshire. This medicine was composed of twenty or more different herbs, but Withering saw that the active one could only be the foxglove. He experimented with this drug, but at first used it in too large doses and for too long. He soon found that the diuretic action did not depend on exciting nausea or vomiting and that it would fail in its effects if it caused purging unless joined with small doses of opium. He discarded the use of the decoction and substituted an infusion, but, later, preferred the powdered leaves.

In 1776 the use of the foxglove was gradually adopted by his medical acquaintances and in 1779 Dr Stokes, of Stourbridge, gave an account of Withering's practice to the Medical Society of Edinburgh, which led to its use in the Infirmary and its inclusion in the Edinburgh Pharmacopœia of 1783. But, as Withering remarked, "It will again be very soon rejected if it should continue to be used in the unrestrained manner in which it has hitherto been used at Edinburgh, and in the enormous doses which it is now directed in London." He records 163 cases observed by himself previous to 1785, as well as many cases reported by others. He preferred the leaves gathered just before blossoming time and instructed that the stalk and midrib should be rejected and the remainder dried in the sun or before a fire. The leaves were then rubbed down to a beautiful green powder weighing less than a fifth the original weight of the leaves. He gave to adults from one to three grains of this powder twice a day, sometimes alone, sometimes with aromatics or in pills with soap or gum ammoniac. He insisted that the doses must not be repeated too quickly, but time allowed for each to take effect, and that it should be continued "until it either acts upon the kidneys, the stomach, the pulse, or the bowels; let it be stopped upon the first appearance of any one of these effects." The

favourable case for its administration was when "the pulse was feeble or intermittent, the countenance pale, the lips livid, the skin cold, the swollen belly soft and fluctuating, or the anasarcous limbs readily pitting under the pressure of the fingers." The drug was chiefly advised as a diuretic, but he noted the powerful action on the heart, that the pulse might be even as slow as 35 in a minute and that "it has a power over the motion of the heart, to a degree yet unobserved in any other medicine, and that this power may be converted to salutary ends." He did not, however, associate this action on the heart with the diuretic effect. His final conclusions were that the digitalis will not universally act as a diuretic, but does so more generally than any other medicine. If it fails, there is but little chance of any other medicine succeeding: in proper doses it is mild in its operation and gives less disturbance to the system than squill or almost any other active medicine; that when the dropsy is attended by palsy, unsound viscera, great debility or other complication of disease, neither the digitalis nor any other diuretic can do more than obtain a truce to the urgency of the symptoms; that it may be used with advantage in every species of dropsy, except the encysted (ovarian cyst), and that it may be useful in diseases unconnected with the dropsy. We undoubtedly owe to Withering the use of this important drug, and his main conclusions remain true to-day; indeed, as Cushny remarked, "It is scarcely an exaggeration to say that the use of digitalis in the early years of the nineteenth century was precisely that prevailing a hundred years later."

In the same year he was elected a Fellow of the Royal Society, and was presented with a diploma by the Medical Society of London. Few foreign savants visited England without paying a visit to Withering. He was now at the zenith of his fame, and his practice extended all over the Midlands and into Wales. During this year his professional journeys amounted to 6353 miles, a remarkable distance

when we consider the state of the roads in those days. This constant travelling could not but be attended with occasional accidents, and once his horses becoming unmanageable, he jumped from his carriage, fractured his collar-bone, and had concussion of the brain. He read and wrote much during these journeys, and carried a light in his carriage for this purpose. His income did not exceed £2000, but he did not seek wealth, and treated large numbers without fees. Until the General Hospital was opened he gave advice to the poor gratis for one hour every day, and the number who applied was between two and three thousand a year.

His botanical work progressed, and he employed two men whose sole business was to collect plants for him all over the country. In 1787 he published a new edition of his *Botanical Arrangement*, and a third volume was added in 1792. Already complimented by the mineralogists, his name was now conferred on a new genus of the Solanaceæ, Witheringia.

In 1790 he suffered from pleurisy, followed by a tedious convalescence, yet he was able to communicate to the Royal Society an "Account of Some Extraordinary Effects of Lightning." Again, in the following year, he suffered from pleurisy, and henceforth his existence was a struggle against his advancing disease, but his mind retained its energy and he persevered in active duties. He was made a Fellow of the Linnean Society, but was unable to take part in their proceedings.

In the year 1791 he was greatly upset by political troubles. A lover of liberty and eye-witness of the grievances which oppressed the French nation, he sympathised with the attempts of the enlightened statesmen who tried to correct the abuses in the government of France, and favoured the popular side, but his hopes were soon shattered and he saw the genius of French freedom "speedily assume the features of a demon and vanish in a shower of blood." Flames of

civil discord broke out at home and in July the Birmingham Riots took place. They were largely the outcome of hatred of one man, Joseph Priestley, whose frankly expressed opinions were obnoxious to the people. On 14th July, about eighty persons of various denominations dined together to commemorate the anniversary of the French Revolution. Priestley was not there, but was known to sympathise with the meeting. Their opponents, the anti-Jacobins, met in a neighbouring hostelry, and drank confusions to Priestley. Their feelings were worked upon by unscrupulous orators and they proceeded to the hotel where the dinner was held, broke all the windows and smashed the furniture. They set fire to Priestley's chapel, the New Meeting House, and also burned the Old Meeting House. The mob then marched to Priestley's house at Fairhill, which was plundered and all the valuable instruments and manuscripts destroyed, Priestley and his family barely escaping.

The next day the houses of several prominent Non-conformists were destroyed, and on the third day eight more. The fury of the crowd remained unabated, and Edgbaston Hall, the residence of Withering, was the next objective. On the night of the dinner at the hotel the doctor had been dining at Birches Green, and returning about eight o'clock, he passed through the crowd collected in the street. When in the midst of them many pulled off their hats and set up a huzza, to which he answered by bowing. Yet next day he had information that his house would be burned on the 14th. He immediately set about the necessary preparations and removed three cart and wagon loads of the most valuable property, drove them into the hayfield and covered them with hay. A mob arrived before preparations were complete, but the resolute action of numerous friends, aided by some famous fighting men hired for the occasion, saved the house from destruction. The opportune arrival of the military soon ended the riot.

These events had a great effect upon his health, and,

together with the difficulty of restricting his engagements, decided him to go abroad. He resigned his hospital appointment in June 1792, and in September left home and travelled by easy stages to Falmouth, where he took ship for Lisbon. Disgusted with the filth of Lisbon, which emitted "a villainous compound of horrid smells," he took a house called St Jozé de Riba Mer, a few miles lower down the river, and there became the centre of an English colony. His health improved and he resumed botanical studies and analysed the waters of Caldas de Rainha, the hot baths of Portugal, for the Government. He returned to England the following May but went back to Portugal for the winter, risking the possibility of being captured by privateers and being carried to France during the reign of terror. His "Memorial of the Caldas Waters" was presented to the Royal Academy of Portugal, and he was admitted a foreign corresponding member. The weather that winter was bad and he did not receive the benefit he had expected, a sharp hæmoptysis occurred in April, and he was advised to return to England. This he did in May, landing at Falmouth, but making a tour of the coast from Land's End to the Isle of Wight before proceeding to Edgbaston; Stonehenge was visited and aroused speculations as to its origin. He noted the difference between the stones of the outer circle and those of the inner; the former being the local grey wethers, but the latter basaltic, which, he thought, could not be found nearer than Antrim. (Modern geologists consider Pembrokeshire the more likely source.) He wrote: "I take it for granted that Stonehenge is neither of Celtic or Druidic origin. It is a structure by far too artificial for such barbarous people and is the work of a much more enlightened nation." He notes the astronomical arrangements, and writes: "The extent of navigation practised by the Phœnicians proves a considerable degree of astronomical knowledge, though it may not be possible to say whether this knowledge originated with themselves or was derived from the Egyptians." He resolves

the matter into the question: "Whether our great astronomical instrument was erected by the Phœnicians or by the ancient Bramins," and hopes that researches into Oriental antiquities will afford an answer. This foreshadows the modern theory of Elliott Smith that megalithic culture was diffused westwards from Egypt through Cretan and Phœnician channels.

His experience of Portugal led him to conclude that "the end of phthisical patients is hastened by removal to hot climates," and that those who were restored to health by judicious attention to the incipient stage of the disorder and by a timely removal to the most favourable parts of the coast of England, recovered as completely and as promptly as such might have done abroad. After remarking on various English stations, he concluded: "The southern shore of the Isle of Wight affords a winter retreat preferable to any other spot in Britain."

Having obtained no benefit from his residence abroad, he decided to remain in England for the following winter, and to create an artificial climate in his library, which he furnished with double sashes, heated by flues and regulated to a uniform temperature of 65°. Although incapacitated from practice by shortness of breath and frequent attacks of hæmorrhage, he re-wrote his botanical work and published a third edition in four volumes in 1796. A long letter was sent to Dr Beddoes, of Bristol, containing many shrewd hints on and reflections on consumption of the lungs. He noted the immunity of workers about lime kilns, butchers, and makers of catgut, and the great prevalence of the disease among the brass casters of Birmingham. He noted experiments on the influence of diet, and described a method for the inhalation of carbonic acid gas which he considered had prolonged the life of many patients.

Withering faced his disabilities with fortitude, and addressed a friend who was in like case, "To encourage a desire to die is an unworthy tendency to desert the post

allotted to us; and if such desires once become motives to make us neglect the means of restoring or preserving health, such motives and such conduct, directly or indirectly tending to cut short our existence are, perhaps, altogether as indefensible and as wicked as the still shorter methods of the pistol or the halter."

During the years 1797-99 his disease, evidently of a fibroid nature, caused increasing dyspnœa, so that his powers of conversation were limited, and the position of writing became at times impossible. In one of his last attacks of pleurisy, we are told that, being unable to obtain a surgeon, he performed venesection upon himself with great composure and dexterity.

He died on 6th October 1799, and was buried in a vault at Edgbaston Church, where on the south side, near the west end, is a mural tablet erected to his memory, enriched with emblems of the Æsculapian art, and representations of the digitalis purpurea and the Witheringia solanacea.

Micheli
Myrica
Olea eu
Pernett
Picea a

Picea m
Pinus c
Populu
Prunus
Prunus
Prunus

Quercus
Quercus
Rhamn
Rhodod
**Rhodo*

Rhodod

**Rhodo*
Rhodod

**Rhodo*
Rhodod
**Rhodo*

Rosa ca
Rosa m

Rosa w
Rubus c
Syringa
Tamari
Thea sp
Thuja c
Vangue
Viburn

CONTENTS

APPENDIX.

LIST OF ILLUSTRATIONS

ORGANIC INHERITANCE IN MAN

INTRODUCTION

THE experimental material of the statesman, physician, and sociologist is the human, a particular kind of animal living in a particular kind of environment. Biology is the science which deals with the nature of living things and with the relation of these to their environment; there is a special biology of the human, a science which seeks to answer the questions as to whence came man, what is man, and whither goes he. It is surely necessary in any attempt to direct the destiny of mankind that those who seek control shall be equipped with a wide knowledge of human biology which concerns itself with the life-lore of the human and with man's relation to the world in which he lives.

One of the most significant facts that has emerged from the study of organic inheritance is that the scientific laws established through experimentation with one form of living organism, apply, with minor modifications, to all the rest. This being so, it behoves those who use the human as experimental material to make themselves acquainted with the generalisations concerning heredity and variation which have been formulated from the results of much critical study of other forms. Man, exceptional in many ways, is essentially similar to those other forms of life which, because of their manifest suitability, have been the experimental material of the geneticist. To-day it is no longer necessary for the geneticist to urge that an understanding of the general principles of his science must necessarily be regarded as a prerequisite to any responsible endeavour to interpret the observed phenomena of human inheritance, and especially

to any attempt to guide the human race towards physical and physiological betterment. This is now an accepted doctrine, and the leaders of the peoples, recognising clearly that only through further developments in science and through the ardent application of the results of scientific investigation to human affairs can humanity hope to achieve its fullest expression, are turning more and more to the scientist for information and indeed for guidance.

The problems of human inheritance must of necessity be studied by methods somewhat different from those which are employed in the case of domesticated animals and plants. Controlled matings are manifestly impossible, and data must be accumulated by the less exact method of analysing family histories. However, it has already been shown quite clearly that many of the physical and physiological characteristics of the human are subject to the laws of inheritance revealed through the study of other forms. The characters of the human which, to many, are of greater importance and interest than the physical, are the mental, and these cannot readily be studied in the case of the lower animals, and even in man himself they are most difficult to define, to measure, and to evaluate. It will be granted that if such qualities as memory, tastes, and intellectual ability, for example, are indeed inherited through the workings of a mechanism by which it is agreed a multitude of bodily characters are transmitted, then heredity must play a decisive rôle in human affairs. Many authorities are prepared to acknowledge that physical and physiological human characters are inherited in a significantly orderly fashion, but regard the psychical qualities as belonging to a totally different category of human attributes, having nothing to do with the hereditary mechanism. It is true that man's mind cannot as yet be measured and analysed as can his body: it is true that the mental qualities are subject to profound modification by training and other environmental influences, for the mind is essentially plastic and educable, so much so indeed that

it is not surprising that many people are convinced that differences in inborn capacity are negligible in comparison with differences in kind and degree of education, so far as their effect upon the ultimate mental attainments of the individual are concerned. It is of the utmost importance that questions such as this should be examined and answered. There is a growing body of critical evidence which tends to show that, on the contrary, inherited differences in mental qualities and capacities do indeed exist and are responsible for much of the observed diversity in human mentality.

Anyone can bring to mind from his personal acquaintances families in which high intellectual attainments, musical talent, mechanical ability, remarkable powers of memory, or the reverse of these, are exhibited. Many attributes seem to run in families and are exhibited by individuals in every generation. Galton, studying this matter critically, examined the family histories of 977 eminent men to find that these were interrelated to a surprisingly high degree. It is recognised that an eminent man is more likely to have eminent relatives than is the average man; that superior ability would seem to be in some measure a family affair; that a superior father is more likely to have a superior son than is a father of ordinary intellectual attainments. For many of us there is a sadness in these conclusions; however, we who cannot produce a pedigree starred with brilliance may find comfort in the thought that perchance we are the first of our lines to exhibit this superiority. To marry into a family; to be born into a family, these are worthy ambitions which would seem to be endorsed by sound biological fact.

The observed facts concerning the inheritance of the less desirable mental attributes most certainly incline one to the opinion that mental qualities of all kinds are indeed heritable, but caution must be observed in considerations of this kind. Such an attitude would seem to disregard the powerful influences which environment and training undoubtedly exert during the period of mental development.

Before such evidence can be accepted, it must be supplemented by more that is precise and definite. Pedigrees in which an unusual number of individuals of subnormal characterisation are present undoubtedly give the impression that something is being inherited, but until all the social conditions that beset the childhood of the individual can be assessed serious doubt must arise as to what particular form of inheritance, social or organic, is responsible for the results.

It is of the utmost importance to note that dissimilar environment does not inevitably disturb fundamental inherited similarity. Members of the same family, the same school, the same community, exposed to the same conditions, retain their individual peculiarities, and it is reasonable to postulate that those who begin by being different, being dissimilar in their hereditary constitution, are never moulded into complete similarity through the impress of environmental agencies. Nature withstands the impress of nurture to a remarkable degree. The same kind and degree of education, this word being used in its broadest sense, do not tend to produce equality among individuals exposed to them: on the contrary, they emphasise the initial dissimilarity. Men are not born free and equal but unequal and bound. The superior in inheritance, being superior, profit more through experience.

The conclusion that to a considerable degree mental attributes, particularly those which involve general ability and capacity, which are essentially polymorphic, are inherited, would seem to be justified, but it must be clearly understood that what is inherited is a capacity, a potentiality, and that which will be developed will be conditioned by environment and training. Many are the talents that are wrapped in the napkins of oblivion and buried because of the lack of appropriate opportunity and of the stimulus towards expression. That which one may be is determined by one's hereditary constitution: that

which one is, is the expression of one's hereditary constitution as conditioned by the forces of environment and education. A person of average endowment who has developed full powers of self-expression is often a more valuable member of his generation than one of greater gifts who, through indolence or lack of opportunity, has allowed them to lie fallow. But it has to be remembered that the latter may be the more desirable parent from the point of view of the race, unless it can be shown that man, by taking thought, can add a cubit to his stature, and that characters thus newly acquired by one generation can be transmitted to the next through the ordinary processes of reproduction.

It is indeed of the greatest importance to decide whether or not an adjustment on the part of the living organism to its environment evokes a character which thereafter is transmitted by the mechanism of inheritance, or whether, on the other hand, advance in this matter of an increase in the suitability of an individual to live more fully in a given environment is not actually the result of some chance variation in the hereditary constitution of an individual which in its origin and cause had no connection with the forces of the environment yet which may, in virtue of its effect upon the general characterisation of the individual, better adjust it to its present or future environment. Critical experimentation thus far has adduced no reason for holding that there is any relation between the origin of a variation and the adjustment which follows. Certain philosophers choose to teach that such adaptive variations are from their beginnings in some sense purposeful. Bergson's conception of creative evolution, in postulating that living matter responds adaptively to new situations as these arise, ignores the manifest fact that many variations are definitely deleterious. The Lamarckian tradition holds that any change in the body may reappear in the offspring, assuming without question that the

hereditary mechanism is of such a kind as can easily be so modified. But modern research has widened the gap between the body and the germ cells which in their union give rise to the next generation, and to-day the hypothesis of the inheritance of acquired characters, *sensu stricto*, is not acceptable. However, efforts are now being made, and with a certain degree of success, to provoke definite changes in the hereditary constitution of an individual at will through the application of a known stimulus and it may not be long before we are in possession of knowledge which will indeed enable us to bring this question of the inheritance of an acquired character into line with other established biological facts. Thus far the geneticist has been concerned with the study of the mode of inheritance of new characters as these presented themselves; he has not busied himself with the problem of the causes of the origin of characters or with the value of these to their exhibitors. To-day, however, he is turning to this subject and is refining his techniques for its investigation. It may be expected that it will be shown that very rarely indeed do environmental agencies provoke modification in the hereditary constitution of a kind and degree as to lead to the repetition through reproduction of characters which have been acquired. It should not be taught that children can possess naturally any and all characters which their parents acquired with effort. It remains to be shown which acquisitions involve a modification of the hereditary constitution of the individual and which do not.

Man may not inherit the bodily or mental attributes which his parents acquired through experience but he does inherit the results of this experience. Memory, speech, the written word, the power of learning during a protracted childhood, the overlapping of the generations, these endow each generation with the acquisitions of its predecessors. Man's social evolution cuts ruthlessly across his slower organic evolution and at times it is well-nigh impossible to

distinguish between these two aspects of human inheritance. Yet it is imperative that such a distinction should be made since man's social evolution may come into conflict with his physical and mental evolution and such a conflict must be avoided if man and his civilisation are to progress.

The bounden duty of one generation is that of ensuring that the social inheritance of the next shall be so shaped that everyone in it may achieve the fullest degree of expression of all the hereditary qualities with which he is endowed and which are advantageous to the individual and to the community. The best material and spiritual environment that man can create is ever necessary. But when this is done, there still remains the problem of man's organic inheritance. The grindstone and the oilstone of civilisation can make nothing of the poor steel of the feebly inherited. The community of to-day must take steps to define social standards that are biologically sound and to ensure that its successor of to-morrow shall be capable of profiting from the improved environment which is being prepared. The present social fabric is full of weak patches which under the present sentimental kind of legislation are protected at the expense of the sound. So long as the general level of inborn qualities is low, so long must the time and energy of the physician be spent in the temporary improvement of the unprofitable; medicine must not be dedicated solely to the repair of the roads along which mankind is being led; it must build new roads, if necessary, which shall lead directly to progressive racial betterment. The map-maker and not the road-mender should be the designation of the physician.

CHAPTER I

THE TWO LAWS OF MENDEL

THE great gap that divides the living from the lifeless has not yet been bridged and science is as yet essentially ignorant of the nature of life, that aggregation of characteristic properties of structure and of behaviour that distinguishes the quick from the dead. It is known that life is always associated with a substance of complex chemical constitution, protoplasm; that the protoplasm of which the bodies of the more highly organised forms of life are built is not a continuous and homogeneous mass, but is divided into definite, though minute, units, the cells, each with its controlling centre, the nucleus. It is known that the body built of these cells has a definite shape and structure, characteristic of the particular species of which the individual is a member. It is known that each individual is the latest member of a long and uninterrupted succession of living things extending back, generation after generation, to the dawn of life, that the spark of life can only be kindled by life itself, and that continuity is the essence of life.

The individuals of one generation age and die, and life is transmitted from one generation to the next through the minutest of channels. Reproduction, the handing on of the torch of life, in the more highly organised living forms, consists in the union of two specialised sex cells, the gametes, the egg elaborated by the female parent, the sperm by the male, to form one cell, the fertilised egg, the zygote, in which the new individual and the next generation has its beginning. The zygote is a new individual, specific to the highest degree, embodying all the possibilities of individual development and of racial perpetuation. Each

of these sexually distinct parents contributes but a single cell, so minute as to be far beyond the vision of the unaided eye, and yet these gametes are the only material links between the generations, and across this narrowest of bridges there must pass everything organic that one generation can inherit from its predecessor.

The zygote presents none of these characters which, when the individual has developed and differentiated, will enable the observer to classify and to describe it and yet in this fertilised egg there are—there must be—something or many somethings that predetermine its morphological, physiological, and psychological destiny. The hereditary constitution of the individual, established at the time of the union of ovum and sperm, decides in great part the future characterisation of the individual; those qualities alone are inherited which are innate in the gametes.

A teacher asked a class the question, "What do elephants have that other animals have not?" One of the class, with the vision that aborts as we grow old, gave the correct and startling answer, "Little elephants." The fact that offspring tend to resemble their parents is so universal and familiar that its significance is forgotten. It is accepted that a great multitude of details of structure and of function is faithfully transmitted from generation to generation; it is recognised that none of these characters are to be seen in the fertilised egg but are assumed as the individual develops. If there is a material basis for this inheritance, then in the gametes must be carried the something that determines what kind of thing shall develop from the product of their union. One of the problems of the science of genetics, which seeks to account for the similarities and dissimilarities in characterisation exhibited by individuals related by a common ancestry and to define the exact relation of successive generations, is that of determining the manner in which the hereditary characters are represented in the fertilised egg and to demonstrate the way

in which these characters become expressed as the development of the individual proceeds.

For centuries it has been recognised that like tends to beget like, and yet among individuals related by a common ancestry there is everywhere recognisable, and often measurable, dissimilarity; that it can be anticipated confidently that every individual born will exhibit, sooner or later, those details of structure and of function which characterise the species, the race, even the family or strain to which he and his ancestors belong, and yet that no son is the carbon copy of his father, that every individual is indeed the first and last of his identical kind. It is established that variation is universal. Much of it is undoubtedly due to the impress of environmental agencies upon the developing body and mind, but much is the reflection of inborn dissimilarity and cannot be ascribed to such a cause.

Variations, dissimilarities in characterisation exhibited by related individuals, are of several kinds, and are due to many causes. For purposes of discussion they may be classified in several ways. They may be *paravariations*, dissimilarities due to differences in environmental impresses, nutritional, climatic, and so forth, being therefore acquired modifications. They may be *mixovariations*, dissimilarities due to differences in hereditary constitutions resulting from the shuffle and the deal of the hereditary factors in breeding; these are the expressions of different combinations of hereditary factors. They may be *idiovariations*, dissimilarities due to mutation, to definite alteration of the hereditary constitution; such are the "sports." The first category — paravariations — is *exogenous*, of environmental origin; the others are *autogenous*, originating within the organism. Paravariations, modifications, are non-heritable differences between related individuals caused by the unequal influence of similar or dissimilar environmental agencies. When studied statistically, they display the normal variability curve.

Variations can be classified according to the nature of their effects upon the organism; they may thus be *morphological*, *physiological*, *psychological*, and *ecological*. Morphological variations are dissimilarities in size and form: physiological are differences in quality and performance; ecological are dissimilarities which result from their fixed relation to dissimilar habitats.

Variations can be classified according to the degree of difference between them: they may be *continuous*, fluctuating, taking the form of a little more or of a little less, or they may be *discontinuous*, widely separated one from the other.

Variations can be classified according to the direction they would seem to take. They may be *fortuitous*, chance variations leading nowhere in particular, or they may be *orthogenetic*, seeming to form a progressive series tending in a definite direction.

In the study of variation the really important decision that must be made is whether a particular difference between related individuals is of environmental or of genetic (autogenous) origin. This can only be decided by the analysis of the results of controlled matings.

It is a fact, established by reliable experience, that certain of the characters of an individual are truly inherited in virtue of the organic relationship of parent and offspring. A man is a sample of *homo sapiens* not because subsequent to his conception he was reared as a human but because he was born of woman. Uncritical impressionistic, but interested, observation has always noted, for example, that a man might, in respect of his eye colour, resemble not his parents but his maternal uncle; in respect of the curl of his hair, his grandfather; if he showed any signs of ability, his father would at once preach a doctrine of direct organic inheritance, and out of such anecdotes, accumulated in family histories, and supported by the more thoughtful accounts of breeders of domestic stock, there slowly but surely arose the notion that in them there were definite suggestions of an orderliness,

a regularity, an interrelationship. It became manifest that the inheritance of characters was not haphazard, but was subject to certain rules. Then it became inevitable that the human mind in its inherent desire to trace and to describe order in Nature should seek some mechanism which in its workings could account for such orderliness.

So the idea of an "idioplasm" (Nageli and others), a special substance the function of which was to transmit and control the hereditary characters, details of form and of function, in the developing individual came into being. This idioplasm remained a purely theoretical conception until Roux, out of his work on cell division, was able to point out that many of the functions of this hypothetical substance could be performed efficiently by the nuclear chromatin. Upon this suggestion Weismann modelled his theory of the germ-plasm; but inspiring as his hypothesis was, it was constructed at a time when knowledge of the essential organisation of the cell was still incomplete and insufficient.

The conception of a germ-plasm, when enunciated, impelled thoughtful inquisitive men to seek more critical methods of demonstrating its existence. Mendel, because of the more skilful planning of his experimentation, was more successful than his fellows in collecting critical data exhibiting a significant orderliness, in constructing a tentative explanation to account for this orderliness, and in testing this hypothesis by further critical experimentation and finding it still trustworthy. Then he was able to convert what had been a mere working hypothesis into a scientific generalisation or law which is but a brief statement of some uniform and constant relationship that has been found to hold through a sufficiently large series of natural events.

Mendelism is a scientific theory relating to the distributive mechanism of organic inheritance originally promulgated in 1866 by Gregor Johann Mendel, Abbot of Brunn, to interpret certain phenomena which emerged from the results of his

experimentation in the breeding of plants. Since that time, this theory has been subjected to all manner of tests. It stands to-day, perhaps somewhat refined, but still fundamentally unaltered.

The theory postulates the existence of a number of individual particles of substance in the germ-plasm, each of which controls the development of some particular tissue or character in the developing organism. It does not require that these particles shall be concerned solely with hereditary transmission. It demands that in respect of any particular character the individual must receive from its parents, one from each, through the gametes, two factors, either similar or dissimilar according to whether or not in respect of this character the parents were alike or different. It requires that when the individual in its turn elaborates its reproductive cells, into each ripe gamete there can pass one or other but not both of these factors. The gamete has a single set of factors, the zygote a double set, and of these one set has been received from each parent. The zygote may be hybrid in respect of a character or characters, since one or more pairs of factors may include dissimilar mates: the gamete cannot be hybrid since factorially it is simplex. It postulates that the association of dissimilar factors within the zygote is not attended by any adulteration effect upon them.

Mendel, experimenting with his peas, founded a science because he was a certain kind of man who applied a certain kind of method and employed a certain kind of experimental material. He kept accurate pedigree records of the ancestry of each individual and of the characterisation of each ancestor; he counted the number of individuals in each generation and the numbers of the dissimilar kinds, and was therefore able to give an exact mathematical statement of his results. He was the first to attempt to reduce the phenomena of inheritance to a measurable basis, employing the exact quantitative methods that scientific discipline demands. He was fortunate in his material, for it gave in his hands

perfectly clear-cut results which made it quite apparent that the mode of inheritance of the characters with which he was dealing could not be a haphazard affair but was surely subject to certain laws, a knowledge of which would enable the experimental breeder to predict the results of his matings. Mendel collected, by observation and controlled experiment, a number of data concerning the phenomena of inheritance sufficient to enable him to recognise the orderliness and regularity of his results. He then constructed a tentative explanation or working hypothesis in order to account for the facts that he had observed and for the apparent inter-relationship of these facts. He then tested his hypothesis by further observation and experiment, and only when it was found to accommodate the facts yielded by this further critical experimentation did his working hypothesis become transmuted into an established scientific law.

The science of genetics deals with heredity, the mechanism by which resemblance between parent and offspring is conserved and transmitted, and with variation, the mechanism by which such resemblance is modified and transformed. It is founded on the two laws of Mendel—the law of segregation and the law of independent assortment and recombination. The law of segregation can be illustrated by the use of the human eye colour characters, brown and blue, if the following statements are accepted without question. Blue eyes mated to blue give only blues: brown eyes × brown give only browns, if the brown have had only a brown-eyed ancestry. If, however, brown eyes with an ancestry including blue eyes are mated with blue eyes, then it may be expected that among their offspring browns and blues will occur in more or less equal numbers. If brown eyes of a brown-eyed ancestry mates with blue eyes, then all the offspring will be brown-eyed. If two such brown-eyed individuals out of a brown × blue parentage mate, then their children will be brown and blue-eyed in the proportion of 3 : 1.

There are several points in these results which invite interpretation. How is it that brown × blue gives brown? How is it that the mating of two browns out of brown × blue gives browns and blues? What is the significance of the 3 : 1 ratio?

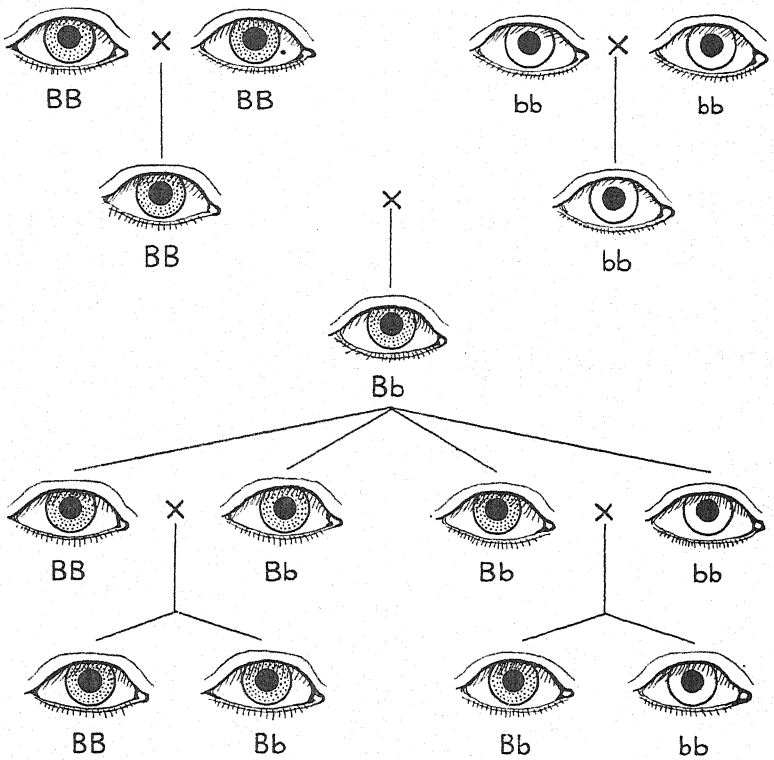


FIG. 1.—Results of the matings of individuals with brown and with blue eyes.

(*stipled iris = Brown : plain iris = blue*)

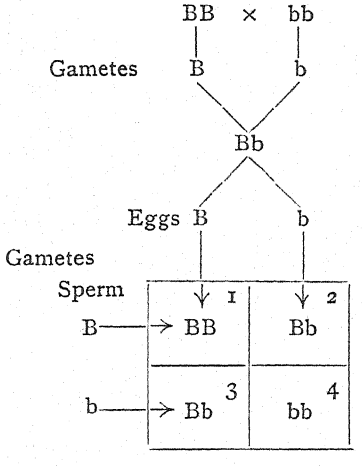
Mendel, to explain identical results obtained from the breeding of the edible pea, put forward the following hypothesis. There are characters which are inherited. Corresponding to these characters there are determiners, hereditary factors, in the gametes which in their union give rise to the individual. Each gamete carries a factor for each

and every heritable character that the future individual may exhibit, and thus the individual, arising in the union of two gametes, has a double set of factors, each gamete, a single set. Characters can be classified as *alternative* (allelomorphic). Thus eye-colour can be brown or blue. Allelomorphic characters are alternative characters of one and the same structure or function. A brown-eyed individual can have received the factor for this character from both parents, being *duplex* for the factor and *homozygous* for the character. On the other hand, this brown-eyed parent may have received one factor for the brown-eye character by way of one gamete and one factor for the alternative character, blue, by way of the other. The individual will then be *simplex* for the factor for brown-eye (and therefore also for the factor for blue), and *heterozygous* for the character exhibited: he or she will be brown-eyed because, for reasons unknown, brown-eye is *dominant* to the *recessive* character blue-eye. A blue-eyed individual is one that is *nulliplex* for the brown-eyed factor and duplex for the factor for the blue-eyed character. This must be so since the simplex condition of the brown factor is enough to produce the brown-eyed character.

Since the gamete is constitutionally simplex, and the individual necessarily duplex, it follows that into each gamete elaborated by an individual there must pass one or other of each pair of factors in the hereditary constitution of the individual. In respect of such characters for which the individual is homozygous, all gametes will be factorially similar, but in respect of those for which the individual is heterozygous there will be two sorts of gametes, one kind carrying the factor for the one character, the other that for its allelomorph, and the two kinds will be elaborated in equal numbers. If of the two characters concerned one is dominant and the other recessive, if in any fertilisation there are available equal numbers of ova carrying respectively one or other of the factors for two alternative characters, and if there are equal numbers of spermatozoa carrying respectively

one or other of the same two factors, and if fertilisation is at random, then chance will yield on the average in every four three individuals exhibiting the dominant character of the pair and one exhibiting the recessive.

Using this hypothesis, the case of the mating brown-eye and blue-eye can be interpreted if the postulated factor for brown-eye colour be represented by B, and that for blue by b. A brown-eyed person, if homozygous, has the factorial constitution BB: if heterozygous, Bb: a blue-eyed must be bb.



First parental generation (P_1).

Into each gamete passes one member of each pair of factors.

First filial generation (F_1).

Brown-eyed since brown is dominant to blue. All heterozygous.

Into each gamete passes one member of each pair of factors. In the case of the heterozygote there will thus be produced equal numbers of gametes of the two kinds of factorial constitution. Two series of such gametes are required.

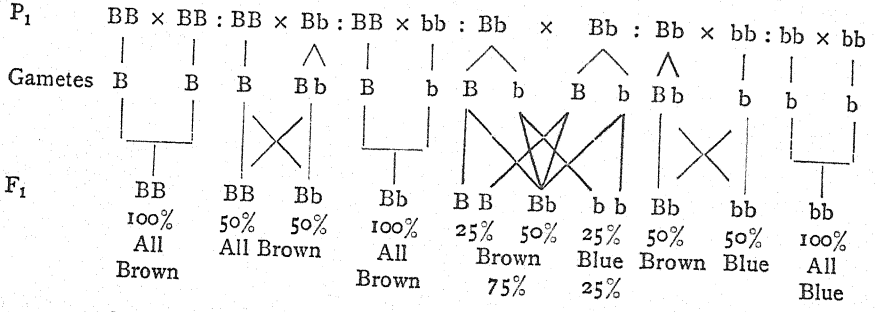
Second filial generation (F_2).

Character classes.	*Factorial classes.*		
B Brown.	BB.	Homozygous browns. Square 1	
	Bb.	Heterozygous browns. Squares 2, 3	3
b Blue.	bb.	Blues (necessarily homozygous for this character, duplex for the factor b, and nulliplex for the factor B) . . Square 4	1

Other matings within this brown-blue series also illustrate Mendel's first law quite clearly. The following matings are possible:—

Homozygous	Brown	(BB)	×	Homozygous Brown	(BB)
,,	,,	,,	×	Heterozygous ,,	(Bb)
,,	,,	,,	×	Blue	(bb)
Heterozygous	,,	(Bb)	×	Heterozygous Brown	(Bb)
,,	,,	,,	×	Blue	(bb)
	Blue	(bb)	×	,, ,,	

The expected results of any of these can be predicted by the use of the checkerboard plan shown on previous page.



A consideration of these expected results, which are confirmed by others extracted from critical observation, will show that the way in which homozygous and heterozygous browns may be distinguished most readily is that which involves their matings with blue-eyed persons. The homozygous brown-eyed individual mating with a blue-eyed will beget none but brown-eyed offspring: the heterozygous brown-eyed, on the other hand, may be expected, in such a mating, to produce both browns and blues. The hereditary constitution of an individual is revealed in the characterisations of the offspring and in the ratios exhibited by the different character groups among these.

The appearance in a generation of equal numbers of individuals exhibiting the recessive character and the dominant character respectively concerned in a particular mating, can only mean that the parents of this generation were heterozygous dominant and recessive respectively. If all the offspring exhibit the dominant character, then the parents can both have been homozygous dominants, one a homozygous and the other a heterozygous dominant, or one a homozygous dominant and the other duplex for the recessive character. If one parent is known to exhibit the recessive character, then the other must have been homozygous for the dominant character.

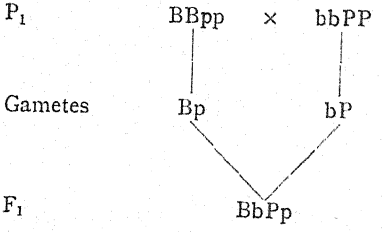
It is now known that the phenomenon of dominance is an unessential feature of Mendelian inheritance. It is, in many instances, not exhibited and the hybrid has a character which appears to be intermediate between those of the two parents; this type of inheritance is known as blending. What is essential, however, is the orderly reappearance in the F_2 generation of the characters of the P_1 individuals and of the F_1 individuals in definite numerical proportions.

Mendel's second law, concerned with the independent assortment of factors, can be illustrated in a consideration of the facts relating to the synchronous inheritance of two pairs of allelomorphic characters. It has been shown that brown-eye and blue-eye are a typical pair of Mendelian characters. Polydactyly and the normal digit number constitute another similar pair, "extra digit" being dominant to normal digit number, the mating polydactyly and normality giving a 3 : 1 ratio in F_2.

It is found that if, for example, a homozygous brown-eyed normally digited individual mates with one who is blue-eyed and (homozygous) polydactylous, the offspring are brown-eyed and polydactylous, *i.e.*, they exhibit the two dominant members of the two pairs of allelomorphic characters. The offspring of two such individuals, having similar family histories, will include, as is shown by data collected from many such families, on the average in every sixteen :—

9 Brown-eyed and Polydactylous.
3 Brown-eyed and normally digited.
3 blue-eyed and Polydactylous.
1 blue-eyed and normally digited.

These facts can be explained by the following scheme. Let P represent the factor for the polydactylous condition and p that for the alternative recessive.



A brown-eyed normally digited individual is mated with a blue-eyed polydactylous.

Into each gamete there passes one member of each pair of factors.

The F_1 individuals are doubly heterozygous, simplex for each of their factors.

Gametes	Eggs BP	Bp	bP	bp
Sperm BP	1 BBPP	2 BBPp	3 BbPP	4 BbPp
Bp	5 BBPp	6 BBpp	7 BbPp	8 Bbpp
bP	9 BpPP	10 BbPp	11 bbPP	12 bbPp
bp	13 BbPp	14 Bbpp	15 bbPp	16 bbpp

Into each gamete there passes one member of each pair. The distribution of the Bb pair is influenced in no way by that of the Pp pair, and so four kinds of gametes are elaborated. Of these there will be two series, ova and sperm. If fertilisation is at random there will be sixteen possible combinations and these will fall into four classes exhibiting the two dominants, one dominant and one recessive, the other dominant and the other recessive, and the two recessives respectively; these classes will appear in the ratio 9 : 3 : 3 : 1.

Character classes. (Phenotypes)	*Factorial classes.* (Genotypes)		
1. The two dominants, B and P	BBPP	. 1	
	BBPp	. 2	
	BbPP	. 2	
	BbPp	. 4	
		—	9
2. One dominant B, one recessive p . .	BBpp	. 1	
	Bbpp	. 2	
		—	3
3. The other dominant P and other recessive b	bbPP	. 1	
	bbPp	. 2	
		—	3
4. The two recessives b and p	bbpp	. 1	
		—	1

In the F_2 generation it is seen that there are all possible combinations of the four characters in the experiment.

There has been dissociation and recombination of the characters during the course of events between the F_1 and the F_2. The 9 : 3 : 3 : 1 ratio follows from the co-existence of two 3 : 1 ratios involved in a single mating.

The ratio in the F_2 of a trihybrid mating, a mating involving three pairs of allelomorphic characters, one member of each pair being dominant, is 27 : 9 : 9 : 9 : 3 : 3 : 3 : 1. It is possible to estimate the ratios for the F_2 of experiments involving 4 or more pairs of characters, but to obtain such ratios is usually impracticable in the case of animals.

Enough has been said to show that if there is a material basis of inheritance, there must be some unit which is

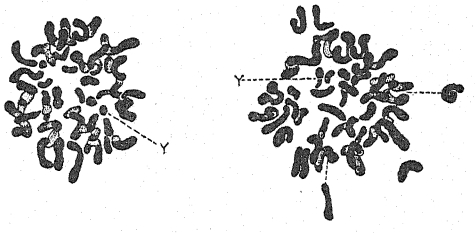


FIG. 2.—The chromosomes of man. *After* Painter.
(*Y = the unequal mate of the X-chromosome in the male*)

structurally continuous through all the cell divisions from the fertilisation of the egg to the liberation of the gametes by the resulting zygote; that these units must be present in duplicate in the fertilised egg; that they must segregate into single components at some point before the functional gametes are formed; and that they must be present in the zygote in pairs.

To-day there exists a very considerable body of knowledge concerning the cell, and it can be stated with confidence that the chromosomes themselves, because they most nearly satisfy the demands made upon the hereditary mechanism by the accumulated facts of experimental breeding, are indeed the germ-plasm, the bearer of the hereditary factors. It has been amply demonstrated that

the only identifiable cell organs that can satisfy these demands are the chromosomes, and that in their behaviour are realised the precise conditions of hereditary transmission as recorded by observation. The modern chromosome theory of heredity postulates that the hereditary factors—the so-called genes—are resident in, are borne upon, the chromosomes, that upon each chromosome is borne a certain association of genes, and that each gene has its own peculiar place upon a particular chromosome. It is possible to indicate a particular point upon a particular chromosome of an individual, and to state that there at this point is the gene for a particular character. It is possible in certain forms, which because of their manifest convenience have been employed as experimental material, to construct a map of their chromosomes which may be likened to a railway time-table, since it shows the sequence of the places and the distances between them. This map gives to the breeder of such a form those powers which are possessed by the synthetic chemist in the manipulation of his materials.

CHAPTER II

THE THEORY OF THE GENE

FOR examples that clearly illustrate the fundamental orderliness and precision of hereditary transmission, it is desirable to turn to the usual material of the geneticist. The fruit-fly, *Drosophila melanogaster*, has been mainly used and to its study we owe the greater part of our present knowledge of the hereditary mechanism. To those living in the years during which this work has been in progress it is difficult, if not impossible, to form a correct valuation of its worth. However, one may be permitted to express the opinion that the name of Thomas Hunt Morgan, Professor of Zoology in Columbia University, will surely be added to those of the immortals of science. He does not merely stand on the shoulders of Mendel, seeing further, he has sprung therefrom to conquer a province of his own.

In fixed and appropriately stained sections of animal and plant tissues, a particularly deeply staining material, chromatin, is readily manifest within the nuclei of the cells. It is to be stated that even yet there exists but little definite knowledge concerning the chemical nature of chromatin; it is known, however, that it is intimately related to the activities of the cell as a whole; that it has a definite architecture and disposition within the nucleus. It is known that during cell division the chromatin becomes condensed and homogeneous and then displays most clearly the nature of its organisation into units, the chromosomes. It is established that the number, size, form, and behaviour of the chromosomes are constant in a species and are

characteristic of that species. It is known that even when the chromatin is thus condensed in the form of chromosomes, it still retains its organic contact with the non-chromatic part of the cell of which it is but a part, though an essential part.

In the body cells and immature gametes of *Drosophila melanogaster* there are four pairs of homologous chromosomes, the members of any one pair being identical in size and shape (with the exception about to be stated). In the ripe gamete, egg or sperm, there are four single chromosomes, and because the chromosomes of the different homologous pairs differ one from the other in their size, shape, and relative position, it can be demonstrated that in the ripe gamete there is present one member of each pair, that in the fertilised egg the diploid (double) number is restored, and that of each reconstructed pair one member has been brought into the zygote by the sperm, the other by the egg. In respect of its chromosomes, the new individual receives from each of its parents one member of each homologous pair.

FIG. 3.—Conventional diagram of the chromosomes of *Drosophila melanogaster*. *After* Morgan.

The chromosome picture differs in the two sexes. In the tissues of the female the members of each pair of chromosomes are identical. In the case of the male tissues one member of one pair is exactly similar in form, size, and disposition to the two members of the corresponding pair in the female, but its mate is unequal, is dissimilar. Since in respect of this pair the sexes differ, these chromosomes in the two sexes are referred to as the sex-chromosomes. The three chromosomes that are alike, two in the female and one in the male, are referred to, for descriptive purposes, as the X-chromosomes, the unequal mate of the X in the male is known as the Y-chromosome. Since of each pair of chromosomes only one can be present

in the ripe gamete, then in respect of the sex-chromosomes all eggs must be alike, each containing an X, whereas there will be two sorts of sperm—the X-chromosome-bearing and the Y-chromosome-bearing. If an X-bearing egg is fertilised by an X-bearing sperm, an XX-bearing zygote will result. The XX type of chromosome content is the female. If an X-bearing egg is fertilised by a Y-bearing sperm, an XY type of individual will result, and this constitution is typical of the male. Here is a simple and satisfactory self-perpetuating sex-determining mechanism.

With this knowledge concerning chromosome constitution and distribution in Drosophila, it is now possible to examine the observed results of experimental breeding and thereafter to demonstrate how these results are to be interpreted in terms of the chromosome hypothesis.

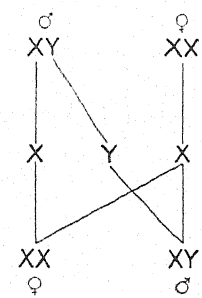
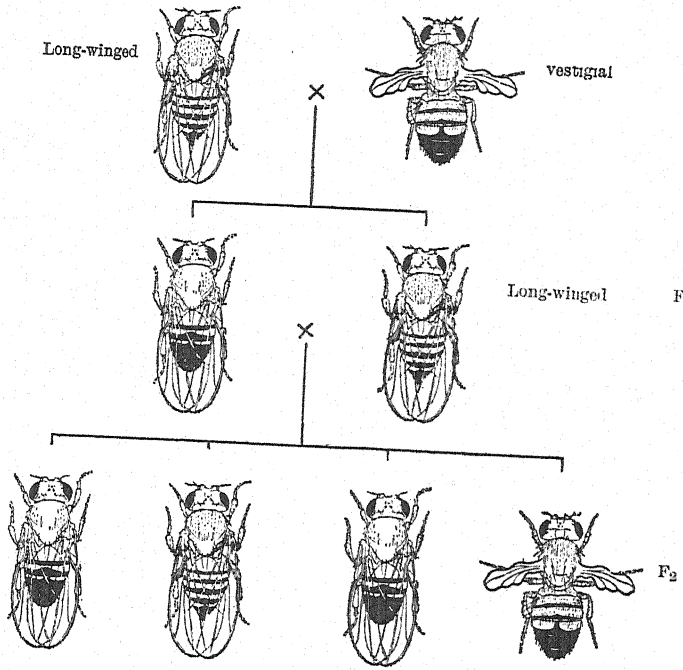


FIG. 4.—The sex-chromosome sex-determining mechanism.

If as a parental generation (P_1) a fly with the wild type "long wings" is mated to one with vestigial wings (this character, "vestigial wing form," appeared as a sport or mutation in a long-winged stock), the first filial generation (F_1) are all long-winged. The character "long-winged" is dominant and in relation to it vestigial is recessive. The significance of dominance is not yet understood. However, in the present argument the occurrence of this phenomenon is of no importance: it is not invariable. The manifest advantage of the dominance-recessivity relation in an experiment is that it permits the transmission of the characters concerned to be traced with ease. If these F_1 long-winged flies are interbred, they will produce a second filial generation (F_2) which includes two classes of flies in respect of wing form—long-winged and vestigial—and in every four on the average there will be three of the former to one of the latter.

The 3 : 1 ratio in the F_2 of an experiment such as that

dealt with above can be explained if the following assumptions are made. The chromosomes are the germ-plasm. In them are resident the agents or factors or genes which in their action determine the future characterisation of the individual, controlling the differentiation of the organs and tissues during ontogeny. There is a gene for long-winged and another



3 Long-winged : 1 vestigial in every 4.

FIG. 5.—A mono-hybrid experiment. Long × vestigial.

gene for vestigial, but only one of these can be present at any time in the particular chromosome that carries them. In each of the chromosomes of a particular pair (the top left pair, let us say) in the long-winged race there is a gene (V) corresponding to the character long-winged; in the case of the vestigial race there is instead a gene for vestigial (v). In respect of the gene content of the remaining chromatin, the two parental forms are regarded as being

identical. Of this particular pair of chromosomes, the F_1 individual will receive one from each parent: one carrying the factor for long-winged, the other that for vestigial. The observed fact is that in their relationship, long-winged is dominant to vestigial. When these F_1 individuals elaborate

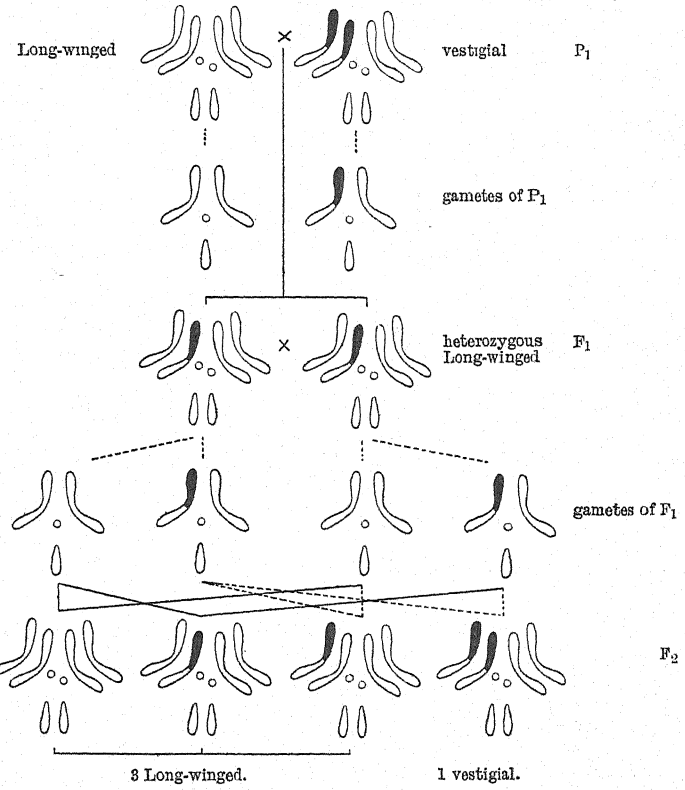


FIG. 6.—The interpretation, in terms of the Chromosome Theory, of the results of a mono-hybrid experiment.

their gametes, into each passes either the chromosome bearing the gene for long-winged or else that bearing the gene for vestigial. If there are equal numbers of the two sorts of eggs and equal numbers of the two sorts of sperm, and if fertilisation is at random, the following chromosome associations will result and the four sorts will be

equally frequent: long-winged : long-winged; long-winged : vestigial; vestigial: long-winged; and vestigial: vestigial. Since the character long-winged is dominant to vestigial, there will be on the average in every four three long-winged flies to each vestigial in F_2.

The mechanism of the distribution of the chromosomes during cell division is one which can accommodate the

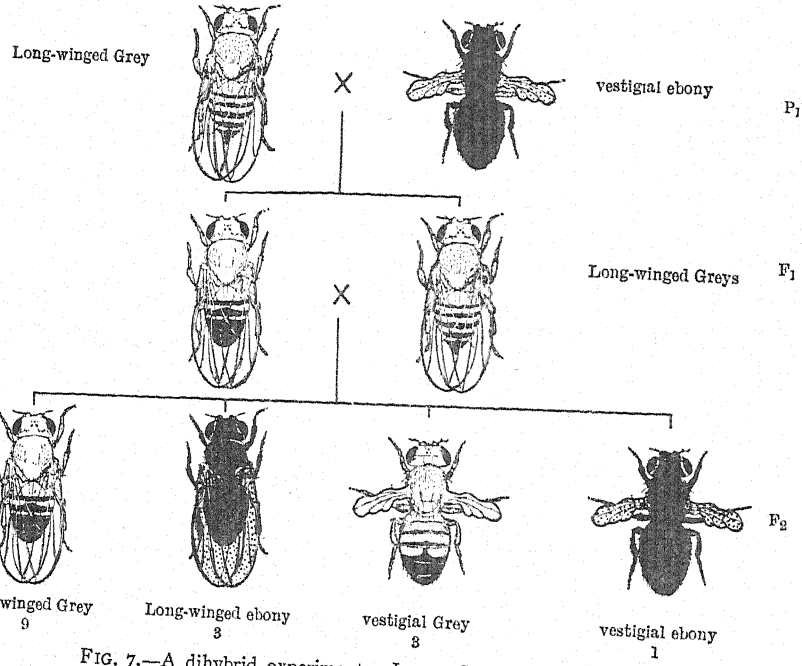


FIG. 7.—A dihybrid experiment: Long, Grey × vestigial, ebony.

observed fact concerning the transmission of the hereditary characters, if within the chromosomes are resident the genes. The gene within the chromosome must necessarily go whither the chromosome passes.

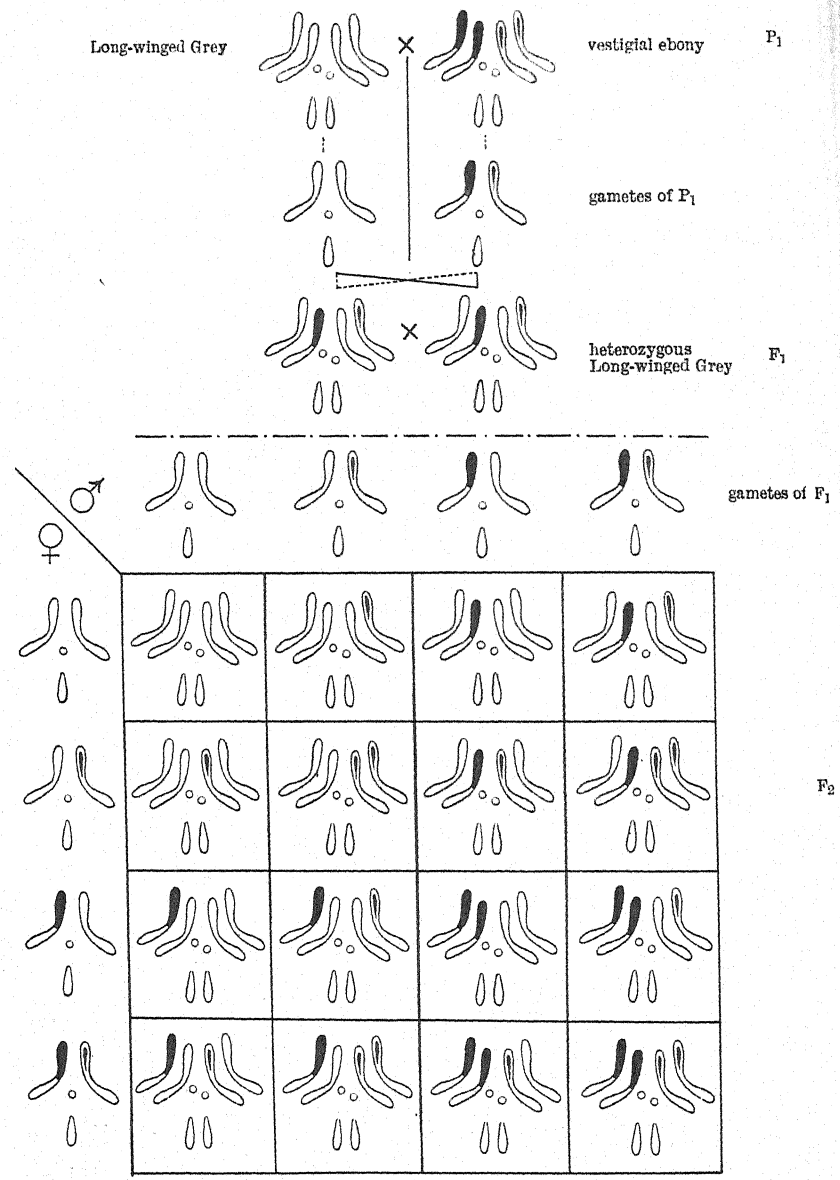
If a long-winged fly, with the wild-type body coloration grey, is mated with a vestigial-winged, ebony-coloured fly (the ebony-coloration appeared as a mutation in a grey stock), the F_1 flies will all be long-winged greys (grey is dominant to ebony). They will exhibit the two dominant

members of the two contrasted pairs of characters. If these F_1 flies are interbred, they will produce four classes of offspring in F_2—long-winged greys, long-winged ebonies, vestigial greys, and vestigial ebonies—and in every sixteen on the average these four classes will appear in the relative proportions of 9 : 3 : 3 : 1. It is to be noted that the two characters of respective parents, long-winged grey and vestigial ebony, have become dissociated and recombined. (Fig. 7.)

The 9 : 3 : 3 : 1 ratio can be explained if it is assumed that the genes for the body-colour characters, grey (E) and ebony (e), are not resident in the same chromosome pair as are those for vestigial (v) and long-winged (V). Two different pairs of chromosomes (V and v; E and e bearing) are concerned (top left and top right respectively). The remaining chromatin in both parental forms is to be regarded as identical. The factorial constitution of the P_1 individuals will be vvEE and VVee respectively; that of the F_1 individuals, VvEe, and these latter will elaborate four sorts of gametes in equal numbers, VE, Ve, vE, and ve. The union of two series of such gametes must yield on the average, in every sixteen, nine zygotes with both V and E (these must be long-winged greys); 3 with V but not E (long-winged ebonies); 3 with E but not V (vestigial greys), and 1 with neither V nor E (vestigial ebonies). (Fig. 8.)

It is again seen that the chromosome hypothesis accommodates the facts. Since the destination of one of the chromosomes is in no way influenced by the distribution of the other, there must be free and random assortment.

If a long-winged grey F_1 male out of the mating long-winged grey and vestigial ebony is mated with a vestigial ebony female, there will be produced four classes of offspring in equal numbers—long-winged greys, long-winged ebonies, vestigial greys, and vestigial ebonies. (Fig. 9.) These results can be explained just as simply. The sperms of the male will be of four sorts (as above) and they will be produced in



9 squares (or zygotes) with genes for both Long-winged and Grey.
3 ,, ,, with gene for Long-winged but not for Grey.
3 ,, ,, with gene for Grey but not for Long-winged.
1 ,, ,, without either of these genes.

Therefore in every 16, 9 Long-winged Grey, 3 Long-winged ebony, 3 vestigial Grey, and 1 vestigial ebony.

FIG. 8.—The interpretation, in terms of the Chromosome Theory, of the results of a dihybrid experiment involving free assortment and recombination.

equal numbers. All the gametes of the female will be alike in respect of the genes for vestigial and ebony. It follows, then, that since vestigial and ebony are recessive characters, the number and proportions of the classes in the resulting generation are predetermined by the number and

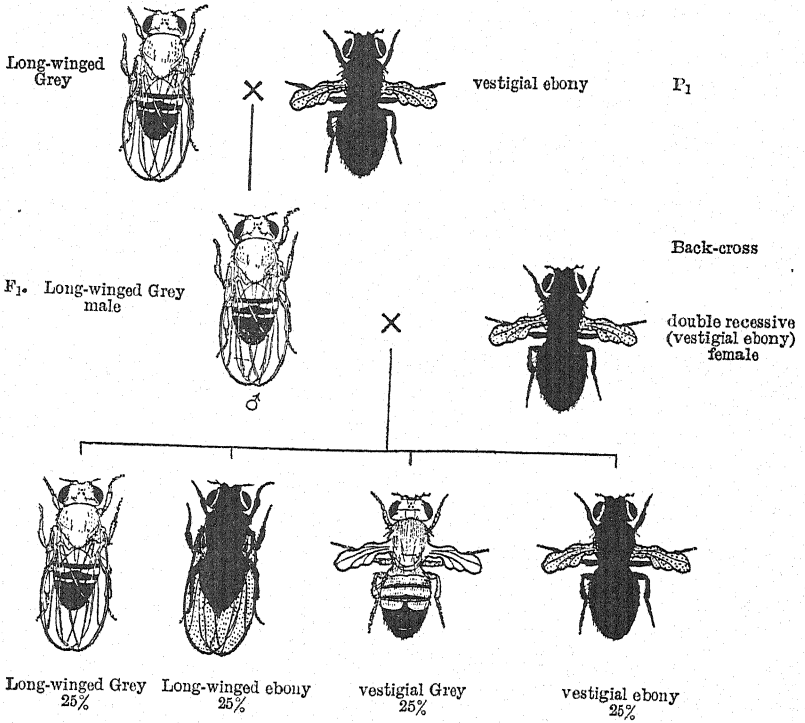


FIG. 9.—Free assortment and recombination in the back-cross of Long-winged and vestigial, Grey and ebony.

proportions of the different sorts of sperm elaborated by the male.

These will be as before VE, Ve, vE, and ve. These fertilising ve eggs must yield long-winged greys (VvEe); long-winged ebonies (Vvee); vestigial greys (vvEe), and vestigial ebonies (vvee) in equal numbers. (Fig. 10.)

It will be recognised that so long as there are as many chromosomes as there are independently heritable characters,

there is no difficulty in accounting for the mode of their transmission, as will be seen from the following table:—

No. of chromosomes in the gamete (the haploid number).	No. of possible combinations of maternal and paternal chromosomes in the zygote.
1	4
2	16
3	56
4	256
5	1,024
6	4,096
7	16,384
8	65,536
9	262,144
10	1,048,576

As there are twenty-four chromosomes in the gamete of the human, it can be seen that infinite variety in the zygote is possible, even though each chromosome bears but a single gene.

In Drosophila there are several hundreds of characters that can be paired off in the same way as vestigial and long-winged, grey body colour and ebony, yet in each gamete there are four chromosomes to bear their genes. It follows that either the chromosome hypothesis fails to satisfy the demands made upon it or else more than one gene is resident in one and the same chromosome. There is no difficulty in making the assumption that if the genes for several different characters are resident in one and the same chromosome, then if that chromosome preserves its integrity during its transference from cell to cell, the characters corresponding to the genes resident therein should be transmitted together and should remain *linked* in inheritance. (Fig. 11.)

As an example of linkage, the following case can be cited. If a vestigial black fly (not ebony, but another mutant character very similar on inspection) is mated with a long-winged grey, all the individuals of the F_1 generation will exhibit the two dominant characters—long-winged and grey. If a male of this generation is mated to a vestigial black

female (*i.e.*, one exhibiting the two recessive characters), only two classes of offspring will appear—vestigial blacks and long-winged greys — and these will be produced in

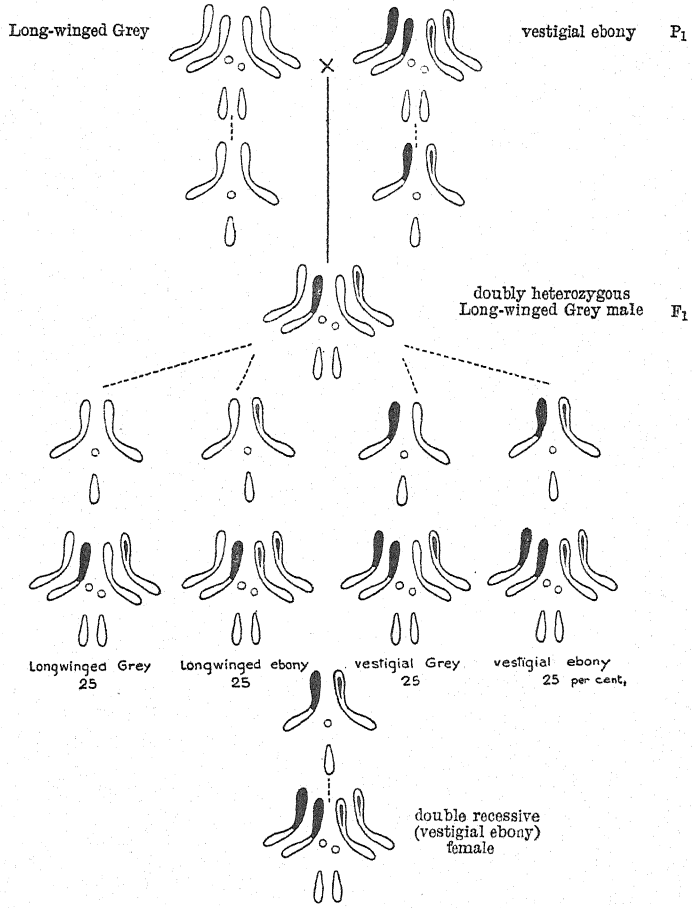


FIG. 10.—The interpretation, in terms of the Chromosome Theory, of the free assortment and recombination of characters in the case of a back-cross.

equal numbers. It will be noticed that the character associations in this generation are exactly those that were exhibited by the two flies with which the experiment started.

If the genes for black and vestigial are resident in one and the same chromosome, then these results can be interpreted. (Fig. 12.)

It has been found that all the characters so far examined in Drosophila fall into four linkage groups. The members of any one group give this 50 per cent. : 50 per cent. ratio

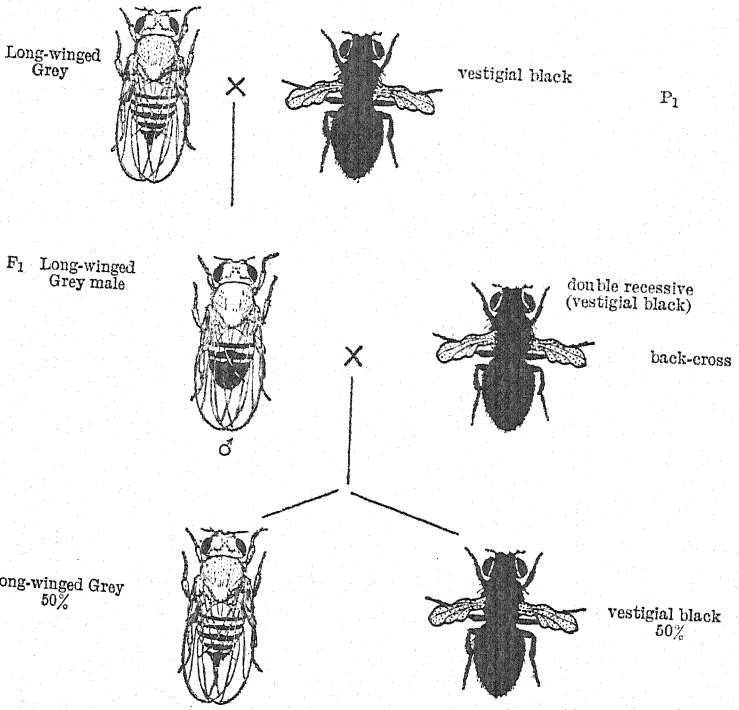


FIG. 11.—Linkage.

when any pair of them are involved in a breeding test similar to that above, but when any one of them is involved in a breeding test along with a member of another group, there is obtained a 25 per cent. : 25 per cent. : 25 per cent. : 25 per cent. ratio, similar to that in the vestigial-ebony experiment described on page 31. There are four linkage groups and four chromosomes. It is reasonable to argue that upon a particular chromosome are resident the genes

of a particular group of characters. More will be said of this conception later.

But linkage does not always hold. The linkage relation can be broken, as is seen in the following example. (Fig. 13.)

If instead of the F_1 male (as in Fig. 11) an F_1 long-winged grey *female* is mated to a vestigial black male,

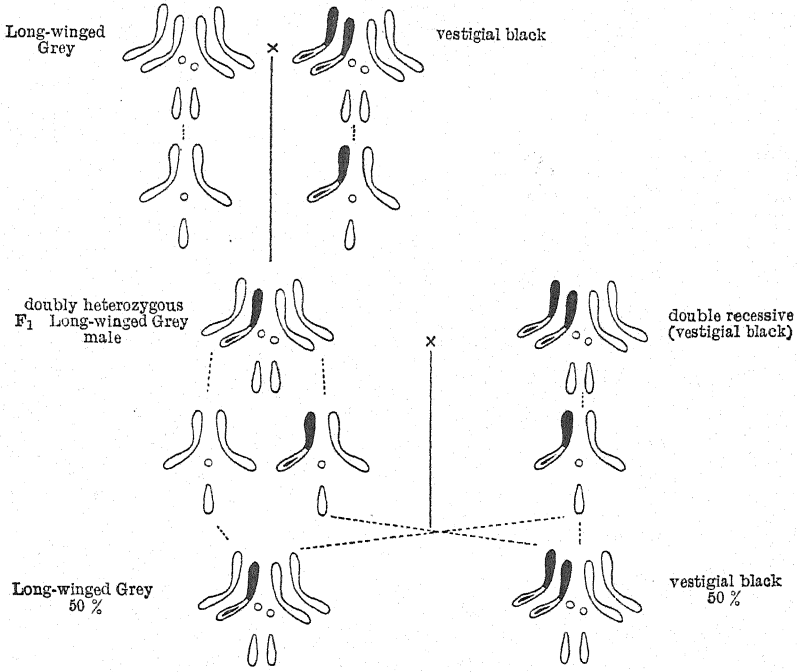


FIG. 12.—Interpretation, in terms of the Chromosome Theory, of Linkage.

then four classes of offspring will be produced, not two as above, and not in equal numbers as in the vestigial-ebony example on page 33, but in the following relative proportions: long-winged greys, 41·5 per cent.; vestigial blacks, 41·5; long-winged blacks, 8·5; and vestigial greys 8·5. It is to be noted that this result differs from that in the case of the mating of the F_1 ♂ to the double recessive ♀ in that there is a dissociation and recombination of characters, but only to a certain limited extent. It is

seen that the 50 : 50 ratio is not obtained when an F_1 *female* is mated with the double recessive. It will be agreed that the reason for the production of four classes of offspring instead of two must be that the F_1 female elaborated four sorts of eggs instead of two, for the sperm of the double

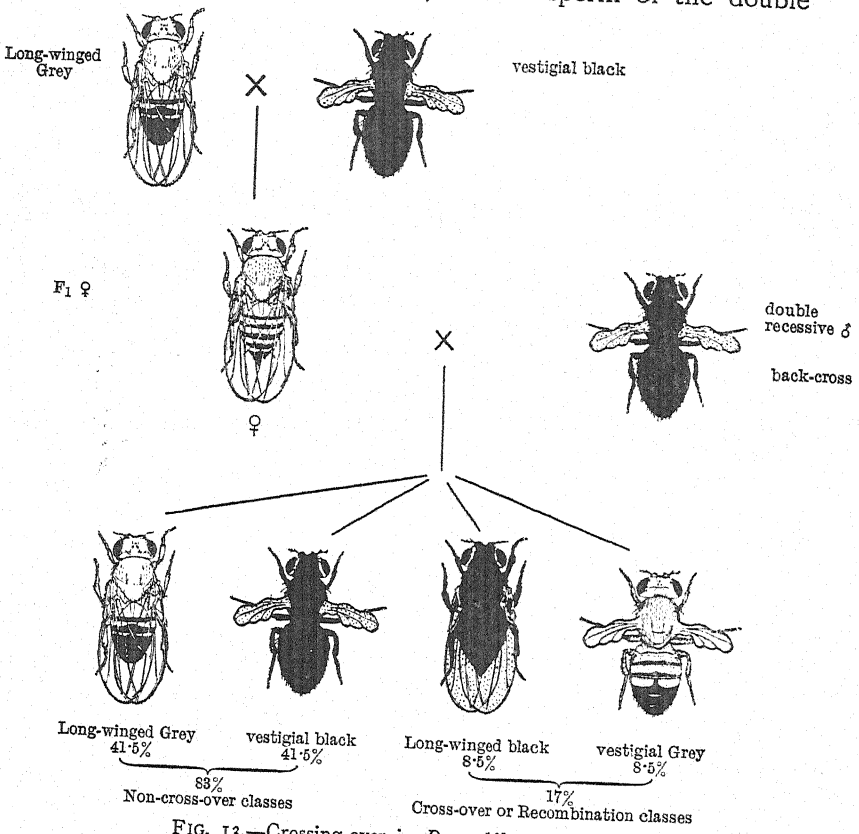


FIG. 13.—Crossing-over in *Drosophila melanogaster*.

recessive male are all alike, and since the characters vestigial and black are recessive, they will not disguise the results. The classes and the proportion of these can be explained if the F_1 female elaborated the following kinds of eggs in the proportions suggested.

B V	b v	B v	b V
41·5	41·5	8·5	8·5

In order that these four sorts shall be elaborated in these proportions, it is necessary that in the maturation of 17 per cent. of the eggs there shall be an interchange of

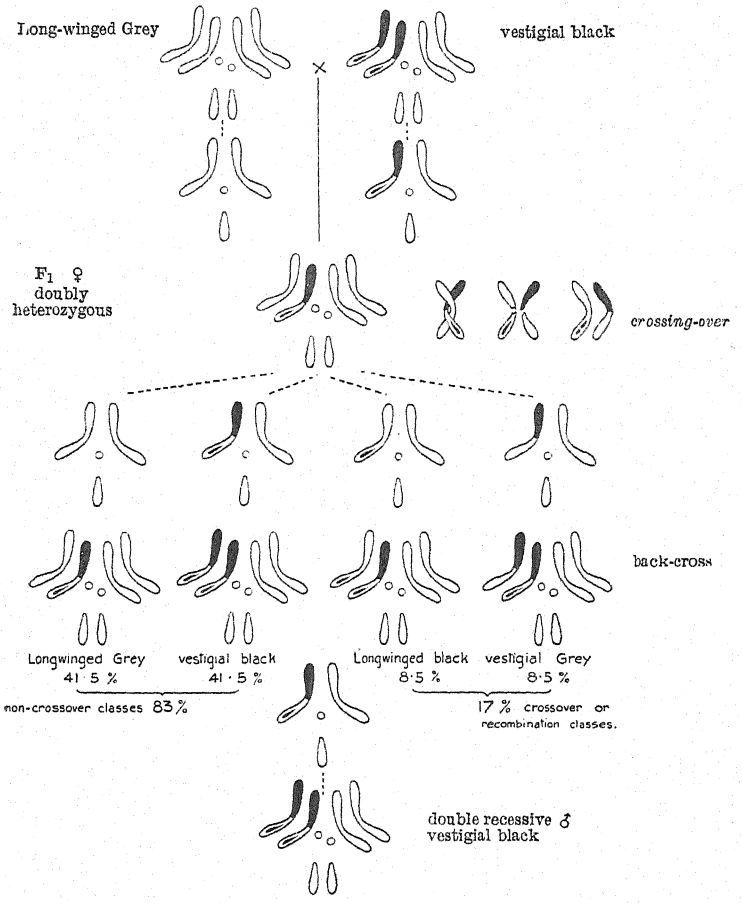


FIG. 14.—The interpretation, in terms of the Chromosome Theory, of Crossing-over.

chromatin between the chromosome B-V and b-v in such a way that the part of the one chromosome carrying the gene B shall be detached from the rest carrying V; that the parts of the other chromosome shall be similarly separated; and that these chromosomes shall then reunite

in such a way that part of one unites with part of the other. It will be noted that interchange leads to significant results only when the chromosomes concerned are dissimilar in their genetic constitution. It is in the case of the *heterozygous* female that such interexchange leads to the production of recombination classes. For reasons at present unknown, such crossing-over does not occur in the case of the male of Drosophila, though it does in that of other forms.

The two new combinations after the interchange has taken place show again the same linkage relations to each other as did the former associations, showing that the linkage relation is independent of the characters that form the combination. Linkage between black and vestigial is exactly similar to that between grey and vestigial, and between black and long-winged. Such an interchange of chromatin between the two members of a pair of homologous chromosomes is known as crossing-over, and the percentage of the recombination or cross-over classes is referred to as the crossing-over value (C.O.V.), whilst the linkage between two genes is expressed by the percentage of cases in which they remain together. If the linkage in a particular case is 50 per cent. and the C.O.V. 50 per cent., the result would exactly simulate the effects of free assortment, giving a 25 : 25 : 25 : 25 per cent. ratio. As a matter of fact, this situation has not arisen in the case of Drosophila, being prevented by the occurrence of double crossing-over—fracture and reunion at two points in the chromosome some distance one from the other.

It will have been recognised that this theory of inheritance, like many of its predecessors, postulates the existence of a number of individual particles of substance each of which controls the development of some particular tissue or character in the developing organism. Like the gemmules of Darwin, the biophors of Weismann, the physiological units of Spencer, the pangens of de Vries, the genes of Morgan are required to be minute yet distinct units of, or

areas in, the chromatin. It is, therefore, of profound interest to know that the chromosomes are indeed made up of small aggregates, the chromomeres. It has been established in favourable cases that a particular chromosome always exhibits the same series of chromomeres in any stage when they can be identified. It has been shown, for example, in the marsupial *Petauroides* that any particular chromosome, to be recognised by its distinctive shape, size, and behaviour, is built up of a definite number of chromomeres, and that these are to be individually recognised by constant differences in form and relative position. The chromosome has a definite and constant organisation.

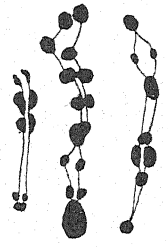


FIG. 15.—Chromomeres in linear series. Conjugating chromosomes of the marsupial *Petauroides*. *After* Agar.

The fact that the chromomeres are arranged in the chromosome in a linear series and that each chromomere has its own particular place or locus in this series is of prime importance in the interpretation of linkage and crossing-over. But it must not be thought that there can be any suggestion that the chromomere itself is the locus or gene.

It is to be understood that the modern theory of inheritance does not require a special idioplasm concerned solely with hereditary transmission. Reproduction is a function of the cell as a whole, dependent, like all its other properties, upon the presence of nuclear chromatin. However, it can be stated that all the evidence there is points to the fact that in the gamete the chromatin alone possesses those attributes of constancy of proportion and behaviour which would appear to be necessary to satisfy the theoretical requirements of an idioplasm.

During the maturation divisions in the production of the gametes the segregation of homologous chromosomes is complicated by the fact that the members of each pair, prior to their separation, become most intimately inter-

twined, and this apparently single, but really double, chromosome then splits longitudinally. This conjugation of homologous chromosomes provides the opportunity for crossing-over. It cannot be shown to have occurred, but if during this conjugation the two chromosomes stick, fracture, and rejoin before separation, then interchange of chromatin will have occurred. It is not without significance that conjugation occurs when the chromosomes are drawn out to their greatest attenuation so that the homologous chromomeres derived from the two parents achieve the maximum degree of association in a linear series. It is seen that the equivalent chromosome contributions of the two parents and their random assortment in maturation and chance recombination in fertilisation, together with the possibility of an inner reorganisation of each chromosome through its most intimate association with another of identical structure but different content, provide an infinite range of new combinations of characters which can be tested out by environmental agencies. The chromosome mechanism can supply the variations upon which the forces of selection can operate. It becomes apparent also that this conjugation of chromosomes in synapsis excludes the possibility of fruitful crosses between species widely different in chromosome constitution.

If the conjugation of homologous chromosomes is accepted as evidence in support of the conception of crossing-over, and if the genes are strung like beads upon a string, each particular gene having its own particular locus upon a particular chromosome, then it follows that the percentage of crossing-over between any two loci can be regarded as an indication of the distance between them. If the members of a pair of homologous chromosomes during their conjugation are as likely to fracture and reunite at one point as at any other point along their length, it follows that the farther apart any two genes lie in the chromosome, the greater is the chance of crossing-over occurring; and

conversely, the nearer together the genes lie, the smaller is the chance of crossing-over occurring. If this is so, then it is possible to construct a map of the chromosomes, showing the relative positions of the different genes resident in each. If A, B, and C form a linear series, and if B lies between A and C, then the crossing-over percentage occurring between A and C should equal the sum of the C.O.V.'s between A and B, B and C. The conception of the localisation of the genes in linear alignment is due to the peculiar differences between the C.O.V. between genes of the same character linkage group. The relation of three or more points to each other is a relation of linear order and cannot be represented in space in any other manner than by a series of points arranged in a line. Linearity is the expression of a system in which there is a fixed succession of elements. The distance between any two elements is constant, but is variable throughout the series. In the case of the more simply organised forms of life, it is possible to conceive the germ-plasm having the form of a congeries of chromatin units, the members of which can exist separately within the nucleus and become associated by chance. In the more complex forms, however, the precision exhibited in the inheritance of a most complicated characterisation demands a very precise and more complex hereditary mechanism, such as is supplied by the chromosomes in their constitution and behaviour.

In order to learn how the chromosome map is made, let us assume, for example, that the recessive character dachs (short legs) appears as a mutation in a stock of Drosophila. Breeding experiments show that it is an hereditary character, for, when mated to the wild type, it gives a 3 : 1 ratio in F_2. We then, let us say, mate a grey normal-legged individual with the new form, black dachs, to get an F_1. The F_1 male is then back-crossed with a double recessive female, and we get a 50 : 50 ratio. We then know that dachs belongs to the same linkage group

as does black. The F_1 female then back-crossed with a double recessive male gives black dachs, 41·25; grey normal, 41·25; black Normal-legged, 8·75; grey dachs, 8·75 per cent. The C.O.V. between dachs and black is 17·5 per cent. We already know that the C.O.V. between black and vestigial is 17 per cent. We can, therefore, anticipate that the C.O.V. between dachs and vestigial will be either 0·5 or 34·5 per cent., the actual figure being decided by the relative positions of the three genes. If a normal-legged long-winged fly is mated with a dachs vestigial, and the F_1 male mated to the double recessive female, a 50 : 50 ratio will be obtained. Dachs is in the same linkage group as vestigial. If the F_1 female is mated with the double recessive, it is found that the C.O.V. between dachs and vestigial is 34·5 per cent. It can now be stated that the relative positions of dachs, black, and vestigial are in the order given, black coming between the other almost exactly midway.

The steps of this experiment are shown in greater detail on the opposite page.

One per cent. of crossing-over is taken as the unit for expressing linkage relations. This unit can be represented in a diagrammatic map of the chromosomes as 1 cm. or any other convenient size. A line is drawn to represent a chromosome. A horizontal mark across it is made to represent the position of the gene for black. Seventeen units of distance to one side of it another mark is made for the gene for vestigial, and 17·5 units to the other side of it one for the gene for dachs. The making of the map is begun. Some 107 genes require to be placed in this chromosome. Their characters all show linkage with black and vestigial and dachs and with each other, and the C.O.V. between any two of them is characteristic. Out of crossing-over work with them it is soon possible to arrange them all in their proper order. In the other linkage groups of Drosophila there are at present some 70,106 and 3 characters respec-

1. P_1 Normal-legged × dachs

F_1 Normal-legged

Normal-legged	dachs
3	1

∴ A typical Mendelian character differing from normal-legged in respect of a single factor.

2. P_1 Normal-legged Grey × dachs black

F_1 Normal-legged Grey

Backcross F_1 Normal-legged Grey ♂ × dachs black ♀

Normal Grey	dachs black
50%	50%

∴ Linked with black.

F_1 Normal-legged Grey ♀ × dachs black ♂

Normal Grey	dachs black	Normal black	dachs grey
41·25%	41·25%	8·75%	8·75%

8·75% + 8·75% = 17·5% = C.O.V. between dachs and black.

3. dachs—black—vestigial

17·5% (dachs—black) + 17% (black—vestigial) = C.O.V. between dachs and vestigial = 34·5%

or black—vestigial—dachs

17% + 17·5% = = 0·5%

P_1 Normal-legged Long-winged × dachs vestigial

F_1 Normal-legged Long-winged

Backcross (*a*) F_1 Normal Long-winged ♂ × dachs vestigial ♀

Normal Long-winged	dachs vestigial
50%	50%

(*b*) F_1 Normal Long-winged ♀ × dachs vestigial ♂

Normal Long-winged	dachs vestigial	Normal vestigial	dachs Long-winged
32·75%	32·75%	17·25%	17·25%

17·25% + 17·25% = 34·5%

The linear order of these three genes is therefore Dachs, Black, and Vestigial.

tively. All that remains is to show which particular chromosome carries the genes for a certain character linkage group.

If a white-eyed male is mated to a (wild type) red-eyed female, all the F_1 males and females alike will be red-eyed,

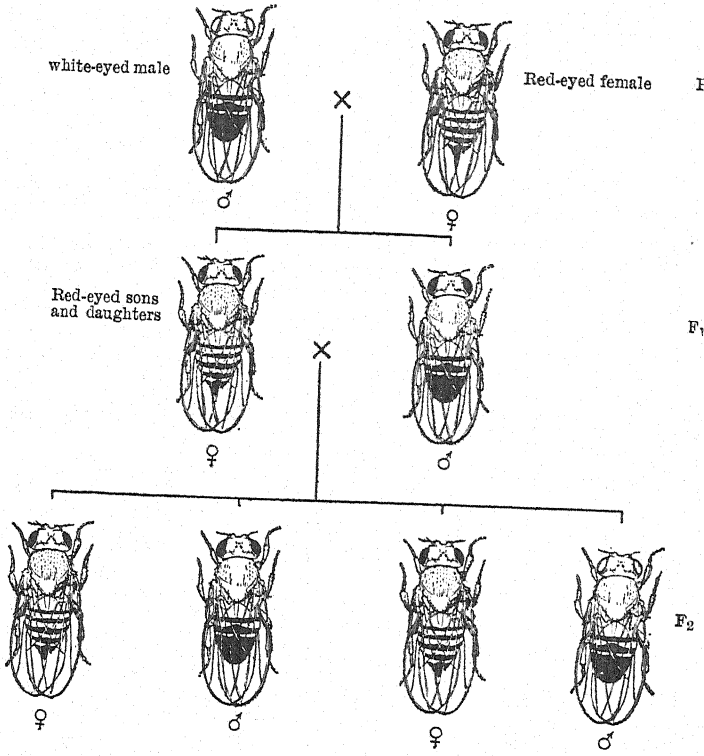
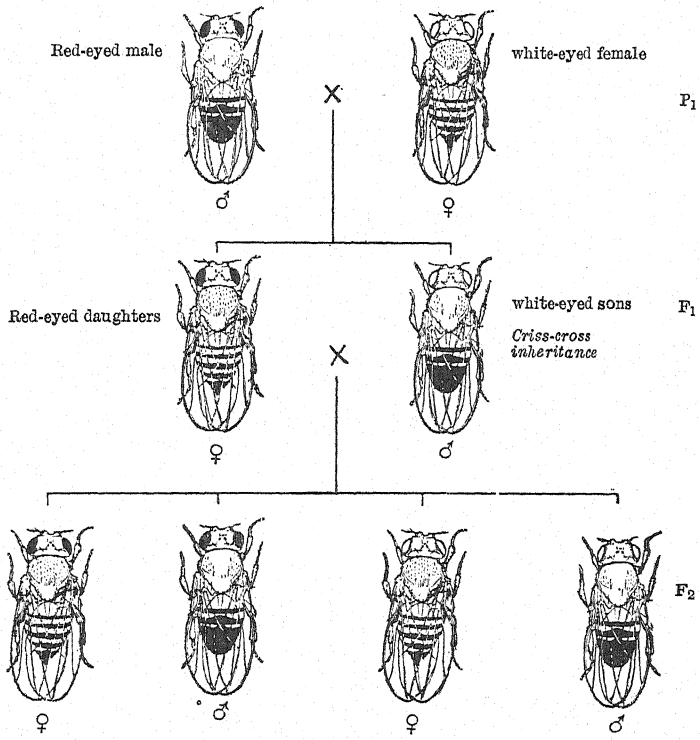


FIG. 16.—Sex-linked inheritance in *Drosophila melanogaster*.

and if these F_1 individuals are interbred, the F_2 will consist of three reds to one white in every four on the average but all the white-eyed individuals will be males. The recessive character of a grandfather is exhibited by none of his children, by none of his granddaughters, and by only 50 per cent. of his grandsons. (Fig. 16.)

If, on the other hand, a red-eyed male is mated to a

white-eyed female, then all the males of F_1 will exhibit the white-eye character of their mother, whereas all the F_1 females will exhibit the red-eye character of their father. There will be criss-cross inheritance, sons "taking after" their mother, daughters after their father. (Fig. 17.)



Equal numbers of males and females and of Red-eyed and white-eyed.

FIG. 17.—Sex-linked inheritance in *Drosophila melanogaster*. The reciprocal cross.

A consideration of these facts will lead to the conclusion that the characters red- and white-eye are being transmitted from generation to generation by some mechanism which is also concerned in the determination of the sex of an individual, and that the simplest interpretation of the facts can be made if it is assumed that the male, in respect of the

elements of the sex-determining mechanism, elaborates two sorts of sperm, one the X-chromosome-bearing, the other the Y-chromosome-bearing; that in the X-chromosome are resident the genes for those characters which in their inheritance behave as does white-eye, being sex-linked; and that in the Y-chromosome there are no genes which

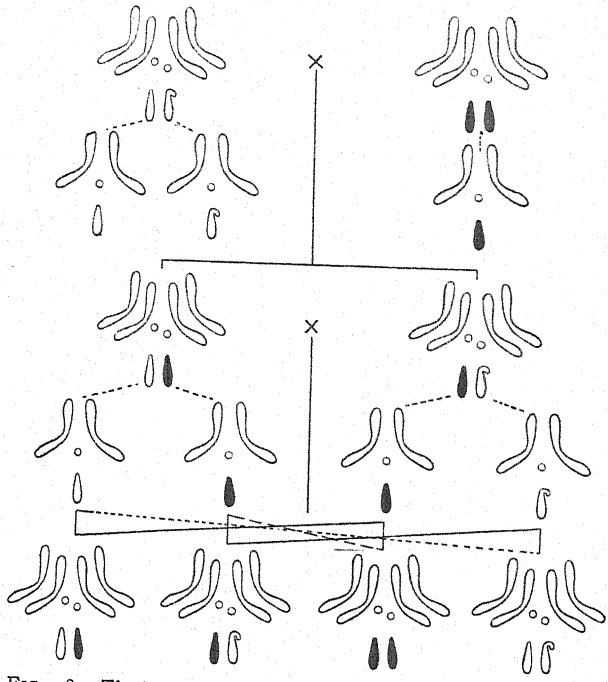


FIG. 18.—The interpretation, in terms of the Chromosome Theory, of the results of a mating involving sex-linked characters.

affect the expression of such characters. In Figs. 18 and 19 the solid chromosome is the X carrying the gene for red-eye, the open one the X carrying the gene for white-eye, the hooked chromosome is the Y of the male; XX is a female, XY a male; red is dominant to white.

It can be accepted that the X-chromosome (chromosome-I) bears the genes of the sex-linked group of characters. It can be shown that the small, round, centrally placed chromosome (chromosome-IV) carries the

genes for another group of linked characters. Individuals with but a single IVth chromosome (Haplo-IV's) and others with three instead of two (Triple-IV's) have been identified, and these abnormalities in chromosome number are associated with definite abnormalities in general characterisation. On chromosome-II, one of the larger boomerang-shaped chromo-

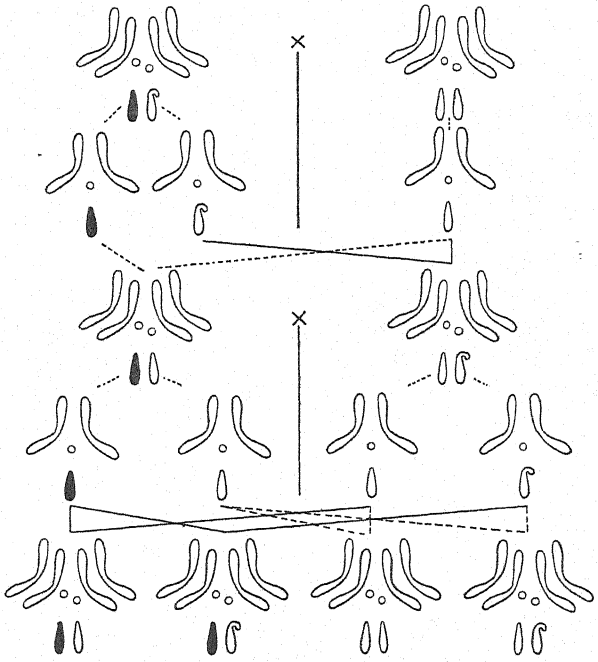


FIG. 19.—The interpretation, in terms of the Chromosome Theory, of the results of a mating involving sex-linked characters. (Reciprocal cross.)

somes, are placed the genes for the characters linked with the character black; on the other large curved chromosome, chromosome-III, those linked with the character Star.

The "gene," a conception as reasonable and as real as the atom, is to be looked upon as a particular state of organisation of the chromatin at a particular point in the length of a particular chromosome. It is a particular area of the chromosome (a locus) in a particular state. This particular condition of this chromatin can be replaced by

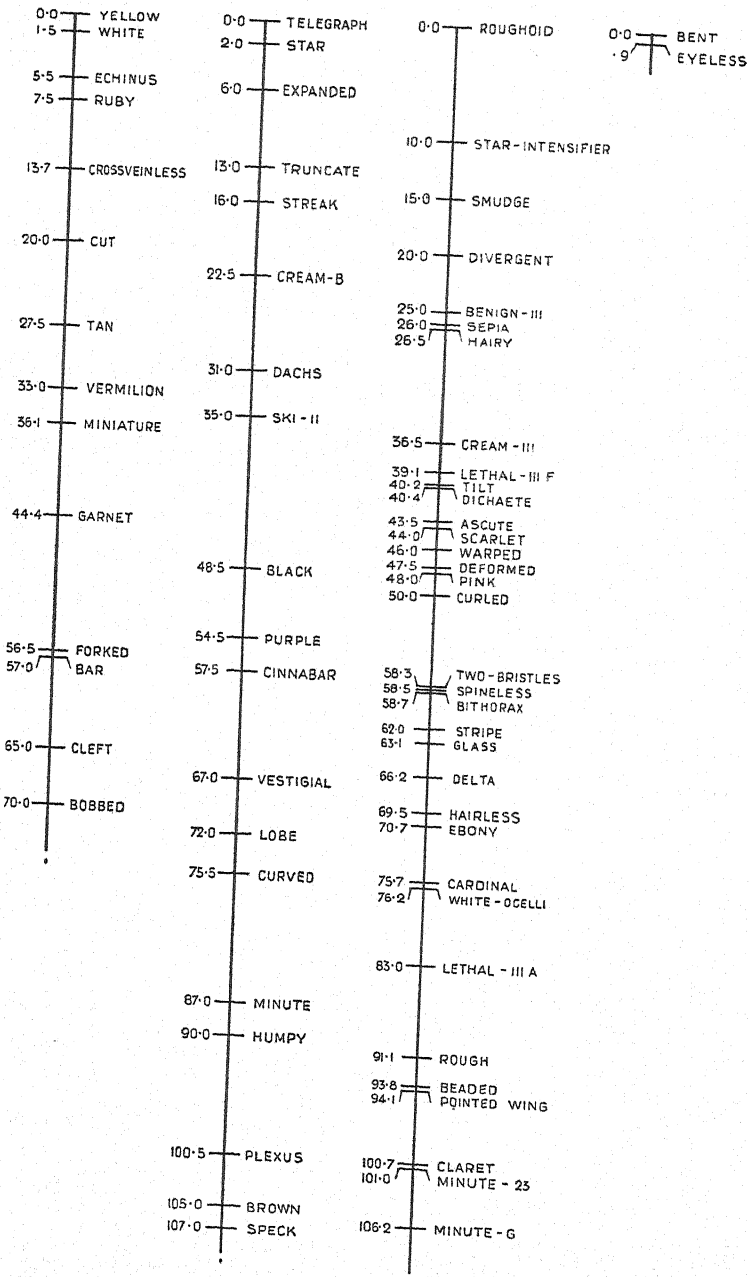


FIG. 20.—The map of the chromosomes of *Drosophila melanogaster*. *After* Morgan.

another, by many others, and with each change another gene appears.

It has been calculated that there may be as many as 2000 distinct loci in the chromatin of Drosophila. The total volume of the chromosomes of *Drosophila melanogaster* is about 0·236 cubic microns. The locus will then be about 61/1000 of a micron in diameter. Another method of calculation suggests 20/1000 of a micron, another 77/1000. The diameter of a molecule of hæmoglobin is $2\frac{1}{2}$/1000. The size of a locus is, therefore, rather larger than that of certain protein molecules.

The chromosome theory of heredity states (1) that the hereditary characters of the individual are referable to paired elements (genes) in the germinal material which are held together in a definite number of linkage groups; (2) that the members of each pair of genes separate when the germ-cells mature in accordance with Mendel's first law and in consequence each germ-cell comes to contain one set only; (3) that the members of different linkage groups assort independently in accordance with Mendel's second law; (4) that an orderly interchange—crossing-over—also takes place, at times, between the elements in corresponding linkage groups; and (5) that the frequency of crossing-over furnishes evidence of the linear order of the genes in each linkage group and of the relative position of the genes with respect to each other.

In man, as has been stated, there are 24 pairs of homologous chromosomes. If that which applies to Drosophila holds also in the case of the human, and there is every reason to postulate that it does, then in man there are 24 groups of linked characters and there are infinitely greater opportunities for crossing-over between the chromosomes. It is not likely, therefore, that linkage (save sex-linkage) will be quickly or readily recognised and it can be expected that man will exhibit an exceedingly great variety in his characterisation. The map of the

chromosomes of man will not be made yet awhile, if ever. But the lack of such a map of man should not prevent an appreciation of the maps of Drosophila and of other forms. The making of the map is not as important as the proper appreciation of its significance.

The theory of the gene has been constructed out of the observed facts of experimental breeding. The facts of cytology are to be regarded as confirmatory evidence of the validity of this theory. Cytological investigation has demonstrated the duality of the chromosome complex of the zygote and the reduction to the haploid number during the maturation of the gametes. In the behaviour of the chromosomes during maturation stages of gametogenesis there is to be observed an exact parallelism to the events postulated by Mendel's first law. A chromosome derived from the paternal parent becomes separated from its mate derived from the maternal parent, and each gamete that results contains one member of each pair of homologous chromosomes of the zygote. If Mendelian factors are substituted for chromosomes the Mendelian argument is presented. It has been shown in suitable forms that the distribution of the chromosomes is at random, that the distribution of the members of one pair is in no way affected by that of the members of any of the others. There is a demonstrable free assortment and recombination of the chromosomes exactly similar to the free assortment of the hereditary factors as postulated by Mendel's second law. Further, it is a fact that so far no case is known in which there are more groups of linked characters than there are chromosomes to carry their genes. It is not without significance that as far as the cytological evidence is concerned, the chromosomes remain intact throughout their history. This is required of them if they are to be used in any interpretation of the phenomenon of linkage. It is true that there is no conclusive cytological evidence of an orderly interchange of chromatin material between the members of a pair of

homologous chromosomes such as is required for the interpretation of crossing-over, but it is reasonable to hold that in view of the genetic evidence concerning this phenomenon sooner or later such interchange will be demonstrated. The results of genetic and of cytological investigation have been obtained independently and the relation of the two cannot be regarded as coincidence: the fact that cytology is endorsing the genetical interpretation of the phenomena of organic inheritance is to be regarded as evidence of the validity of such interpretation.

Evidence from other sources that the chromosomes are indeed the bearers of the hereditary factors has been accumulating at a rapid rate during recent years. It has long been established that inheritance is biparental and that the important contribution of the male lies within the head of the spermatozoon. It is not without significance that it is reasonable to hold that the essential constituent of the head of the sperm is the chromatin. It is significant also that segmentation of the ovum does not proceed in the absence of at least one full (haploid) set of chromosomes and that although a haploid set of chromosomes can be associated with the production of an individual of normal characterisation, as far as can be judged, such individuals are physiologically imperfect.

The most convincing evidence concerning the significance of the chromosomes in inheritance is that which has emerged from the results of the study of the specific effects upon the general characterisation of changes in the number of chromosomes in cases in which each of these carries genes corresponding to characters which in their transmission enable the observer to trace the chromosome from generation to generation.

It can be shown, for example, by genetic and cytological methods, that the small round chromosome-IV of Drosophila is sometimes absent from one of the gametes, having been lost by some accident in distribution during gametogenesis.

If an ovum lacking the chromosome-IV is fertilised by a sperm of normal chromosome content, including one chromosome-IV, a "haplo-IV" fly develops which in its characterisation is markedly different from the normal diplo-IV fly. It is a small pale individual which hatches late, and has a dark trident and small slender bristles. The wings are blunt and but slightly spread, and the eyes are large and rounded. Thus it is evident that the presence or

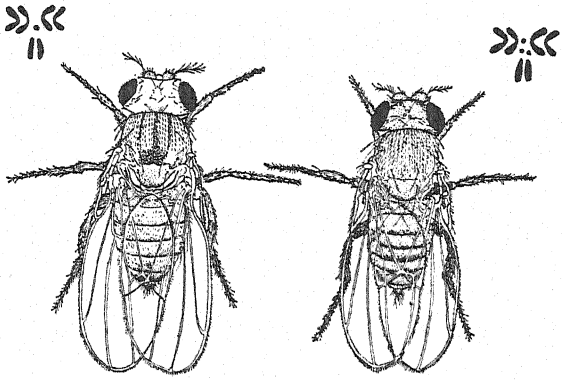


FIG. 21.—Haplo-IV and Triplo-IV individuals. *After* Morgan.

absence of one of these chromosomes makes all the difference to the ultimate characterisation.

The gene for the character "eyeless" is resident in chromosome-IV. If a haplo-IV is mated to a diplo-IV eyeless male, half of the offspring are eyeless. These have developed from eggs with no chromosome-IV fertilised by sperms with a chromosome-IV carrying the gene for eyeless. Many of these eyeless flies fail to hatch, and this fact is to be interpreted as the result of the action of the gene for eyeless. The action of a gene is not restricted to a single effect: the gene for eyeless is so named because the eyeless condition is the most readily recognised of its effects, but it also affects the general physiological worthiness of the whole individual, rendering it less viable.

In other cases chromosome-IV is present in triplicate. Such triplo-IV flies differ markedly from ordinary diplo-IV's: the eyes are smaller, the wings narrower, the body colour darker. If a triplo-IV is mated to an eyeless fly, two classes of offspring result. Half are triplo-IV's and half are

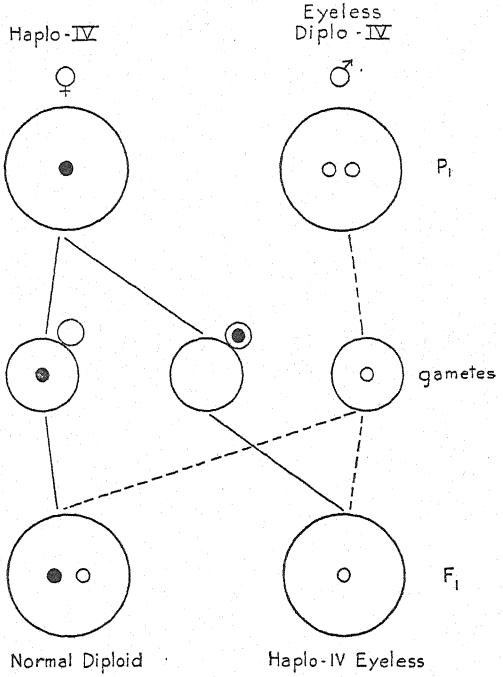


FIG. 22.—The interpretation, in terms of the Chromosome Theory, of the results of the mating of Haplo-IV and Diplo-IV, eyeless. *After* Morgan.

normal diplo-IV's. If one of these triplo-IV's is then back-crossed to an eyeless, five normals to each eyeless are obtained in the resulting generation instead of equality as in the ordinary case in which a heterozygous individual is back-crossed to a recessive. This 5 : 1 ratio is that which would be expected in view of the distribution of the chromosomes.

Evidence showing the reasonableness of placing the

genes corresponding to sex-linked characters upon the X-chromosomes has already been presented. The dissimilarity of the X and of the Y-chromosomes in the male in Drosophila renders the mode of inheritance of characters,

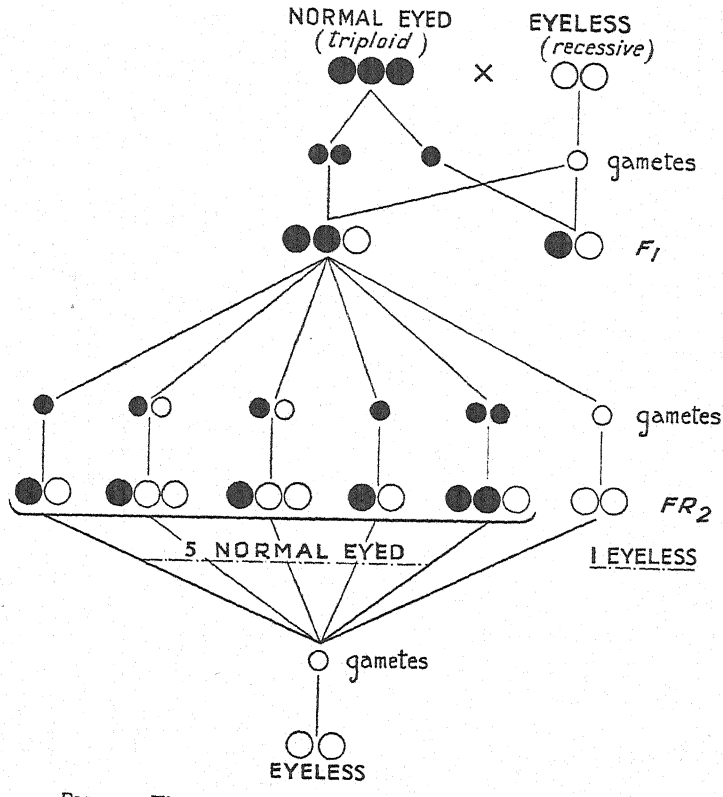


FIG. 23.—The interpretation, in terms of the Chromosome Theory, of the 5 : 1 ratio. *After* Morgan.

the genes for which are resident in the X, somewhat different from that of any of the characters the genes for which are autosomal. The Y-chromosome does not carry any genes which conceal any recessive genes in the X, and save that it is a mate for the X during the reduction divisions of the spermatozoa, it can be disregarded. It has been established that the transmission of the sex-linked characters follows the

distribution of the X-chromosomes. It will be remembered that when a red-eyed male is mated to a white-eyed female, the sons are white-eyed and the daughters red-eyed. Such criss-cross inheritance is characteristic of such a mating involving sex-linked characters. But fairly frequently there appear among the offspring exceptional white-eyed daughters and red-eyed sons.

Cytological examination of such exceptional white-eyed females revealed that the dividing nuclei of their cells displayed a Y element in addition to the normal pair of X's. The condition was that of *secondary non-disjunction* and can be interpreted on the assumption that at reduction of the egg in which this individual had its origin, the XX pair, in exceptional cases, failed to *disjoin*, so that the mature ovum contained either two XX or none. An egg which possesses two X's instead of one may be fertilised by an X-bearing or a Y-bearing sperm, and so the resulting zygotes may come to have three X elements or two X's and a Y. An XXX individual is a female; an XXY individual is also a female although it possesses a Y-chromosome in addition to its two X's. An egg which possesses no X-element at all can be fertilised by an X-bearing or a Y-bearing sperm to form an XO or an OY individual, and of these an XO individual is a male, quite normal in appearance but sterile; an OY does not develop. The type of non-disjunction consequent upon the failure of the two X-chromosomes to disjoin is known as *primary non-disjunction of chromosome-I.* The type of non-disjunction consequent upon the presence of an extra sex-chromosome is known as *secondary non-disjunction of the sex-chromosomes.* Except for an unusual sex-ratio, the presence of such (cytologically) exceptional males and females would not be suspected in one and the same strain; but should such a non-disjunctional female be employed in a sex-linked experiment, the appearance of exceptional phenotypes would indicate what had happened. For example, the mating of a red-eyed male

and a white-eyed primary non-disjunctional female would give the following results:—

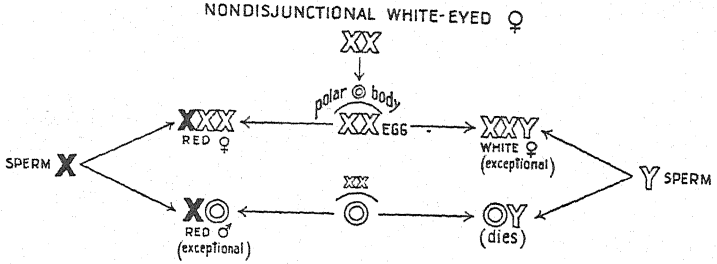


FIG. 24.—Primary Non-disjunction. *After* Bridges.

In the case of the XXY white-eyed female, it is to be assumed that when homologous chromosomes pair in synapsis, two types of reduction division are possible. If the X's conjugate, then in reduction they disjoin and pass to opposite poles and the Y-chromosome will pass to one or the other pole. Thus X and XY ova will be produced in equal numbers. If, on the other hand, an X conjugates with the Y, then X and Y pass to opposite poles where one of them will be joined by the other X. Thus X, XX, XY, and Y ova will be produced.

The ova of an XXY white-eyed non-disjunctional female may then be of four sorts associated with four sorts of polar bodies. If this female is white-eyed, there can be no gene for the red-eyed condition in her genetic constitution and the genes for white-eye are borne upon the X-chromosomes. If her ova are fertilised by the sperm of a red-eyed male (the gene for red-eye being carried on the single X-chromosome) the history of her chromosomes which bear the gene for white-eye can be followed. (Fig. 25.)

The exceptional white-eyed daughters of the non-disjunctional XXY female and the red-eyed XY male are white-eyed because they do not get one of their X-chromosomes from their father; the exceptional red-eyed males are red-eyed because they get their Y-chromosome from their mother and their X from their father.

Thus the non-disjunction of the X-chromosomes can explain the entire series of the exceptional genetic phenomena which occur in these strains. When once a non-disjunctional female is present in a stock, unusual results must accumulate in increasing proportions. The experimental breeding results, endorsed by the cytological evidence, turned what seemed to be in direct contradistinction to the interpretation of sex-linked inheritance in terms of the chromosome theory of heredity into a most spectacular confirmation of this theory. A consideration of

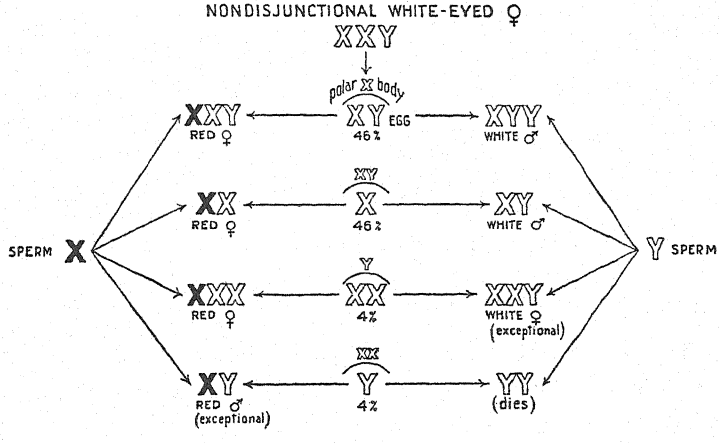


FIG. 25.—Secondary Non-disjunction. *After* Bridges.

the results of non-disjunction will show how chromosome aberration can lead to dissimilarity in the characterisation of closely related individuals. The irregularities in the distribution of the chromosomes may be of various kinds and occur in all probability during the maturation division of the gametes. The migration of the chromosomes to the poles of the dividing cell may be irregular, so that the two daughter cells come to possess an abnormal number. The essential feature in chromosome aberration is the quantitative abnormality in the chromosome content as opposed to the qualitative abnormality in the case of mutation.

The conclusion that the genes for the sex-linked characters are resident in the X-chromosome is supported by yet another instance of aberrant chromosome distribution. A type of female appeared whose genetic behaviour could be explained only on the assumption that her two X-chromosomes had somehow or other become attached so that her eggs received either both X-chromosomes or

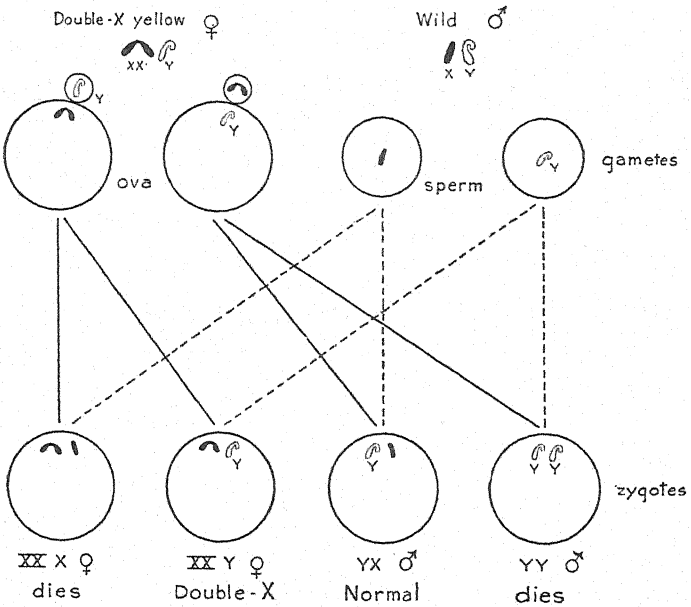


FIG. 26.—The interpretation, in terms of the Chromosome Theory, of the case of the adherent X-chromosomes in Drosophila. *After* Morgan.

none. Cytological examination showed that indeed the two X-chromosomes were joined end-to-end and that there was in addition a Y-chromosome present. It so happened that these exceptional flies were yellow-bodied and so the distribution of the X-chromosomes bearing the genes for this sex-linked and readily recognisable character could be traced. The expected results of the mating of such a fly are shown in the diagram below. Two kinds of eggs are to be expected, one egg with two X-chromosomes each carrying

the gene for yellow, the other with the Y-chromosome and no gene for yellow. If these eggs are fertilised by sperms from any male, preferably one with recessive genes in his X-chromosome, four kinds of offspring should appear and of these two should die. Those that are viable should be the XXY yellow female like the mother, and an XY male like the father in the matter of his sex-linked characters

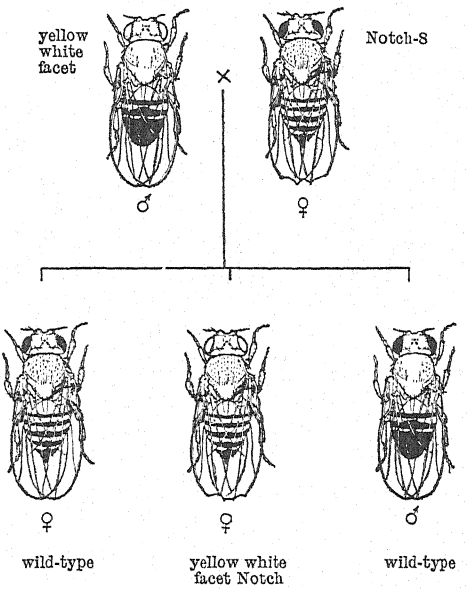


FIG. 27.—The inheritance of Notch-8. Deficiency. *After* Mohr.

since he gets his X-chromosome from his father. This is exactly what happens.

There is a mutation known as Notch-8, the gene for which lies in the X-chromosome. This mutation affects not a single locus but a definite and measurable section of the chromosome near the north end which includes the loci of the genes for the characters white, facet and abnormal abdomen situated at 1·5, 2·7, and 4·5 morgans (units of distance) from yellow. In the female heterozygous for the characters Notch, white and facet (Fig. 27), in spite of the

fact that the latter two are recessive characters, they were exhibited, and the reasonable interpretation of this fact is that which is based on the assumption that the section of the other X-chromosome from 1·5 to 2·7 had become physiologically inactive. A section of the X-chromosome

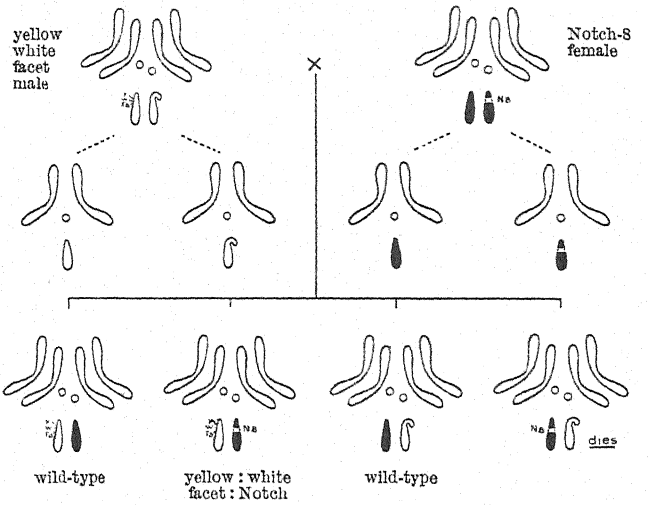


FIG. 28.—The interpretation, in terms of the Chromosome Theory, of Deficiency. *After* Mohr.

of about 4·7 morgans is affected by this mutation as is shown by crossing-over experiments, crossing-over not occurring within the abnormal section. Suchphy siological inactivation is known as deficiency.

Further instances showing the relation of the chromosome number to the ultimate characterisation of the individual will be given in the discussion relating to the determination of sex.

CHAPTER III

THE MECHANISM OF SEX-DETERMINATION

SEX is the term used to define that differentiation of different parts of an individual, or of the same individual at different times, or of different individuals, which is associated with the elaboration of physiologically and often morphologically dissimilar gametes in the union of which the next generation of individuals has its origin. Maleness is the state or quality associated with the elaboration of spermatozoa (or of their physiological equivalents); femaleness is the state or quality associated with the elaboration of ova (or of their physiological equivalents). Sexuality is the state or quality of being distinguished by sex. A male is an individual that exhibits the state or quality of maleness, one that is efficiently equipped for the elaboration of functional spermatozoa and for the conveyance of these towards the site of fertilisation; a female, one that exhibits the state or quality of femaleness, one efficiently organised for the elaboration of functional ova, for the conveyance of these to the site of fertilisation, and often for the prenatal accommodation of the zygote, the fertilised egg, for the transit to the exterior of this new individual at some stage of its development and for the nurture of it thereafter. If in a group (*e.g.* a species) it is customary for maleness and femaleness to be exhibited by one and the same individual, coincidently or in succession, the group and the individuals comprising it are monœcious, hermaphrodite, though it follows that in certain cases an individual can at one time be a male and at another a female. If in a group it is not customary for maleness and femaleness to characterise one and the same individual the group is diœcious, bisexual;

the sexes are separate and every individual within the group is throughout its sexual life either a male or else a female.

Sexuality is an attribute of the function of reproduction; it is concerned with the capacity of living things to multiply. Sexual reproduction, distinguished by the preliminary process of fertilisation, requires that two physiologically and in many instances morphologically dissimilar gametes, derived, in most cases, from dissimilar areas of one and the same individual, or from two separate and sexually distinct individuals, shall unite to form a zygote in which the new individual shall have its beginning. It is to be noted that in the non-cellular Protozoa, as well as in the Metozoa, there is in sexual reproduction a reduction of nuclear material, and following this, a fusion of nuclear material derived from different sources.

Sexual reproduction is practised by all forms of animal life, and it is reasonable to assume that it is beneficial to the race. It would appear that the reproductive elements of the individual body are not involved in the general bodily functioning, in the processes of individuation, but lie dormant and protected within the body, specially reserved for their own particular destiny. They constitute the material chain that binds the generations and are in a sense immortal. It can be shown in favourable instances that this segregation of the reproductive elements is a fact, and it is probable that it is so in all groups of organisms. In *Ascaris megalocephala* it has been possible to demonstrate that the first division of the fertilised egg results in two cells which can be recognised from the beginning as being different in their organisation; one of these cells gives rise to the somatic tissues and the other to the germ-cells. In the case of the former the nuclear material undergoes a marked diminution in quantity, whereas in the other no such reduction takes place. The lineage of the sex-cells from embryo to adult is demonstrable, and these can be shown to form the material link between the generations.

Bisexuality can be looked upon as the basis of evolutionary

plasticity, since through it mutations that have occurred remotely in space and independently in time can meet to reinforce each other, offering among the number of their random combinations characterisations which, when tested by the selective agencies within their environment, are judged on their merits, the harmful leading to the elimination of their exhibitors. If it is true, as the chromosome theory of organic inheritance postulates, that for all the characters, anatomical and physiological, there are antecedent determiners, factors, or genes, in the germ-plasm, the chromosomes themselves, if new characterisations are but reflections of specific regional alterations in the organisation of the chromatin material, of mutations, and if new characters, having arisen, persist in virtue of the integrity of the hereditary mechanism, then it follows that in allogamy — cross-fertilisation — there exists the mechanism for the spread of a new characterisation through the race to which the individual belongs, since it can be brought into association with other genetic variations, other genetic deviations from the usual characterisation, that have occurred independently in time and remotely in space. This mingling of different hereditary constitutions, of different genotypes, leads to different factorial recombinations, and thence to new character combinations, new phenotypes, these being the raw material upon which selective agencies may work. If for every heritable character there is an antecedent determiner or gene, then this gene may be present in the germ-plasm in the duplex state, having been contributed by both parents, or it may be present in the simplex state, having been contributed by one. All characters are not advantageous; the harmful can, however, be balanced by the helpful. The end-result of a gene in the simplex state may not be so disadvantageous as that of the same gene in the duplex state. A heterozygous individual, possessing the gene (or genes) for a character (or characters) in the simplex state may thus be better fitted to accommodate

itself to the variations of an inconstant environment than the homozygote which, because of the purity of its factorial constitution, is not so plastic. By means of conjugation and of allogamy generally, advantageous genetic acquisitions can be pooled. Equally truly disadvantageous genetic acquisitions can be pooled also, but if it is permissible to speak of advantage at all, it is to the advantage of the race and not the individual that reference is made.

In the great majority of animals every individual is either a male or else a female. Male is commonly to be distinguished from female by differences in the sexual phenotype, the sexual characterisation consisting of (1) the gonads or sex-glands, (2) the accessory sexual apparatus of ducts and associated glands concerned with the transference of the products of the gonads and, in the female of many forms, of the zygote itself, (3) the external organs of reproduction, and (4) certain skeletal and cutaneous and other less definite physiological and psychological characters, often loosely referred to as the secondary and tertiary sexual characters, some of which are employed not directly in sexual congress but in some cases in courtship, combat, concealment, and in the case of the female, in the care and nourishment of the young.

The relegation of the function of reproduction to a specialised system of the individual's body has been attended by the provision of an efficient equipment for sexual congress. In the simpler forms the products of the gonads are merely liberated at the body surface, and the prospects of the fertilisation of the ovum by the sperm are relatively remote; fertilisation is entirely a matter of the chance meeting of dissimilar gametes. The development of the accessory sexual apparatus and external genitalia provided the means for the direct transference of spermatozoa to the genital passages of the female and so rendered fertilisation far more certain. Highly elaborated sexual tropisms, when developed, further increase the certainty of profitable sexual congress, whilst amazingly perfect contraptions have been utilised to

bring the sexes together for this purpose. Care of the young is exhibited by those species in which the production of gametes, particularly by the female, is restricted, and in those cases in which the offspring themselves possess but a limited supply of nutritive material. As a general rule, it seems that the earlier an embryo is forced by its organisation actively to provide for its own subsistence, the more care it needs. The mother in some cases merely protects her offspring, in others she also nurses them. In some cases the young actively seek parental protection, in others the father and not the mother cares for the embryonic young. The parents in some cases carry the developing zygotes in different parts of the body which often take the form of specialised sacs, *e.g.*, the marsupial pouch and the uterus. Oviparity is replaced by viviparity with associated changes in the maternal organism, since it demands internal fertilisation and the anatomical, physiological, and psychological equipment for coitus.

	Sex-dimorphic Characters.	
	Male.	Female.
Primary genotypic characters symbolised as	XY	XX
in action lead to the establishment of an internal environment of initial physiological states, maleness or femaleness, symbolised as	1X : 2A	1X : 1A
In this internal environment *Secondary genotypic characters* become differentiated. These are such as are the direct expression of genetic action. They include :—		
Primary gonadic characters. The physiological action of the gonad reinforces the initial maleness or femaleness, and the	testes	ovaries
Secondary gonadic characters, depending for their differentiation directly upon the physiological action of the gonads, become differentiated. These include :—		
The accessory sexual apparatus . .	Wolffian duct derivatives	Müllerian duct derivatives
The external genitalia . . . . and	penis, scrotum	clitoris, vulva
Certain morphological, physiological, and psychological differences in degree and direction of the development of common anlagen.		

Though attempts to classify the sex-dimorphic characters for purposes of discussion have been many, it has to be confessed that as yet no satisfactory classification exists. That this is so is due to the fact that as yet no exact knowledge exists concerning the genetic nature of many of these characters and of their relation to the sex-glands, and until this has been secured, any attempt to classify them, such as that above, must be premature. For the present, it is enough to hold that the characters which in their combination constitute maleness or femaleness respectively are characters in the genetic sense, being expressions of a genotype that is determined by the nature of the genes brought into the zygote by the conjugating gametes. In the fertilised egg there are none of the characters that distinguish race from race, male from female, that make each individual the first and last of its identical kind; these are expressed as ontogeny proceeds and their expression is modelled, encouraged, embarrassed, to a greater or less extent, by the impress of the agencies of the external environment, the outer world, and by the changing conditions within the developing zygote itself, the internal environment, established by the whole of the genotype in action and by the functional activity of the characters as these become differentiated. As a working hypothesis, it can be accepted that sexuality is primarily based upon antecedent determiners within the germ-plasm, upon genes resident in the chromosomes.

At the beginning of this century it was generally believed that at the time of fertilisation the egg was completely ambivalent as regards the future sex of the resulting zygote; it was customary to refer the sex of an organism to the conditions incident to development. But certain facts of general biology are now known which are not susceptible to interpretation of this kind. They point to the view that sex in the higher animals is usually predetermined at the time of fertilisation. Identical twins, *i.e.*, twin zygotes

derived from a single fertilised ovum, are always of the same sex. Such polyembryony is rare in the human, but in the Texas nine-banded armadillo it is the rule for four young to be produced at a time, all of the same sex and remarkably alike. It has been shown that in the case of the armadillo a single fertilised ovum after development to a certain stage budded off four embryos. On the other hand, in those cases in which the different embryos arise from separate ova, it is known that the individuals are not invariably of the same sex. There is no appreciable reason why, if purely environmental factors are at work in determining the sex of the offspring, litters produced from one egg should be of the same sex, while litters produced from separate eggs should include both males and females. From such observations as these it would appear that the sex of the individual is determined by the constitution of the fertilised ovum at the time of fertilisation.

In an ever-increasing number of instances it can be shown that the phenotypic differences distinguishing male and female are associated with constant differences in the chromosome content of the tissues of the two sexes. This fact is illustrated in the clearest possible manner in the case of *Drosophila melanogaster* which has four pairs of homologous chromosomes. In respect of the sex-chromosomes the female is XX, the male XY. The female of Drosophila is monogametic, the male digametic. When egg and sperm unite in fertilisation, into the zygotes will be received one member of each pair from the father by way of the sperm, the other member of each pair from the mother by way of the egg, and there will be two forms of zygotes, one that received an X-chromosome by way of the sperm and the other that received a Y-chromosome. The first will have a sex-chromosome constitution that can be symbolised as XX, the chromosome constitution typical of a female, the other a sex-chromosome constitution symbolised as XY, that of a male. This sex-determining chromosome

mechanism yields results that are in every way comparable with those that are obtained when a heterozygous dominant (Aa) is mated to a recessive (aa) in a typical Mendelian mono-hybrid experiment—equal numbers of the two classes that were represented in the mating. In respect of the X-borne genes, the male is constitutionally simplex, the female duplex.

The conclusion that a difference in the gametes of the two sexes is correlated with the sex of the future individual is abundantly supported by the results of other cytological research. As early as 1902, it was demonstrated that in various Orthoptera (the crickets, cockroaches, and grasshoppers) there is in the male an unpaired chromosome instead of the equal pair in the case of the female. The constitution of the female in these forms is XX, of the male XO, so that while all the female gametes must contain an X element, only half of the spermatozoa will do so. An egg fertilised by an X-bearing sperm must give rise to an XX type of individual, a female. An egg fertilised by a sperm which lacks the X will give rise to an XO type of individual, a male. In other forms it was found that the number of chromosomes was identical in both sexes, but that, as in the case of Drosophila, while in one sex the X was equally paired, in the other it was paired with an unequal mate; the female is XX, the male XY in some groups; in others, in the currant moth, *Abraxas*, and birds, for example, the female is XY and the male XX.

In a third type of sex-chromosome constitution the X is represented, not by one chromosome, but by a group of any number from 2 to 8, which during gametogenesis act together as a compound X-element. The group is single in the male, double in the female, and these cases, therefore, conform to the XX = ♀, X = ♂ type. If as in certain cases there is a Y-chromosome in addition, this is always single. In other forms the X-chromosome is found to be joined to the end of one of the autosomes, remaining

constantly associated with the autosome throughout the whole of the chromosome cycle.

Sperm dimorphism, estimated by measuring the head length of the sperm, has been recorded in a considerable number of species. It is found that there are two intergrading size classes, and it is assumed that the larger consists of the X-bearing, the smaller of the no-X-bearing sperm. Recently, doubt has been cast upon the validity of these observations.

These facts, reinforced by those derived from the study of sex-linked inheritance, point clearly and directly to the conclusion that sex is determined at the time of fertilisation by a mechanism revealed by the behaviour and distribution of the sex-chromosomes.

The Y-chromosome in Drosophila, a partner to the X-chromosome during gametogenesis, is not concerned in the determination of sex. It would seem that one X, or one "dose" of some sex-determining gene or genes upon the X, normally results in the production of a male, two "doses" producing a female. Sex-linked characters are associated with the sex-determining mechanism because their genes are located in the sex-chromosomes and these characters do not necessarily have anything to do with the sexual organisation of the individual; they are sex-linked, not sex-limited characters, and are mainly concerned in the general development of the body as are most of the characters, the genes of which are placed upon the other chromosomes.

The clearest light is thrown upon the sex-chromosome sex-determining mechanism by the phenomenon of gynandromorphism, which is an intersexual condition due to a regional disharmony in the distribution of the sex-chromosomes.

A gynandromorph is an individual of a bisexual species which exhibits a mosaic of male and female sexual characters; it is a sex mosaic in space. In the case of *Drosophila melanogaster*, about 1 in every 2000 individuals

exhibits this condition of gynandromorphism. Most of these are lateral gynandromorphs exhibiting the complete male characterisation on one side of the antero-posterior mid-line of the body, the complete female characterisation on the other, with a sharply demarcated line of junction of the two kinds of tissue. Since the male body is normally smaller than that of the female, the gynandromorph's body is bent towards the male half. Usually in these cases there is an ovary on the female side, a testis on the male; but this is not always the case, nor would it be expected that it should be, for the gonads are not formed from a single nucleus but from several nuclei which give rise to the primordial germ-cells, and so it is not inevitable that both gonads should be histologically and cytologically similar. Commonly, however, there are two ovaries or two testes in a lateral gynandromorph. In other cases of gynandromorphism one-quarter of the body is male in its sexual characterisation, three-quarters female; in still others less than a quarter is male, while more rarely the head is female whilst the rest of the body and abdomen are male.

Many of these sexually abnormal forms have been described in great detail, and it has been shown that if in the mating that produces the gynandromorphic forms sex-linked characters are involved, and if the sex-linked characterisations of the two parents are dissimilar, then the sex-linked characters of the male parts are those exhibited by the father or those exhibited by the mother, whereas the sex-linked characters of the female parts are a combination of the sex-linked characters of both parents, and that, in respect of the autosomal (non-sex-linked) characters, male and female parts are alike. The example depicted below is a lateral gynandromorph, the left side exhibiting a typical female characterisation, the right a typical male. The left side presents the dominant sex-linked character, Notch (the mother was Notch), and the right exhibits the recessive sex-linked characters ascute,

broadwing, echinus eye, ruby eye, tan body colour, and forked bristles (the father had these characters).

These facts point to the conclusion that gynandromorphism in such a case as this results from aberration in the distribution of the X-chromosomes. If it is assumed

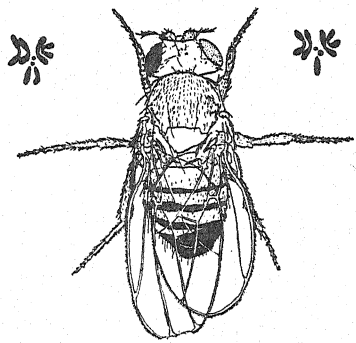


FIG. 29.—A lateral gynandromorph.

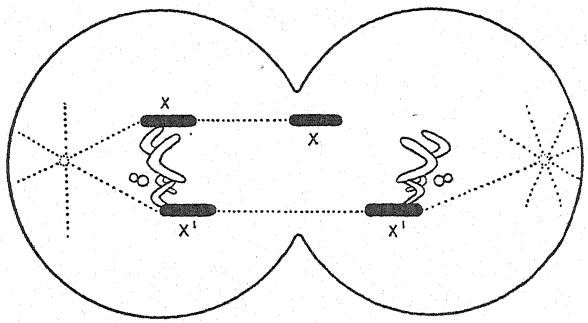


FIG. 30.—Morgan's interpretation of gynandromorphism.

that the gynandromorph is in its beginning an XX-zygote, a genotypic female, and that at some stage during the early cleavage divisions of the fertilised egg a daughter X-chromosome fails to enter one of the daughter cells, this cell will then contain one X instead of two, *i.e.*, will contain the genotype of a cell that normally is XO or XY. Since one X is derived from the paternal contribution of nuclear material, and the other from the maternal, and since, if the

parents were dissimilar in their sex-linked characterisation, these two X-chromosomes will be dissimilar in their gene content, it follows that the characterisations based upon genes in either of them can be markedly different from that based upon the genes in both.

The mother (XX) carries in each of her X-chromosomes the gene for the dominant sex-linked mutant character Notch. The father (XY) carries in his single X-chromosome (X^1) the genes for the recessive sex-linked characters ascute, broad, echinus, ruby, tan, and forked. The F_1 female zygote will receive one X-chromosome from each parent. If nothing untoward happens during ontogeny, she will exhibit the dominant character Notch and not scute, not broad, not echinus, not ruby, not tan, and not forked—the dominants of both parents—and be a typical female. If, however, during the first cleavage division of this zygote the maternal X-chromosome fails to enter a daughter cell, the paternal X^1 alone will be present therein and the tissues that develop from this daughter cell will be 1X : 2A (male) in constitution (where 1A = a complete set (haploid) of autosomes), and cannot be Notch but will exhibit, if they belong to the appropriate parts, the recessive sex-linked characters of the father. If it is the paternal X^1 that is thus eliminated, the male side of the gynandromorph will exhibit the sex-linked character of the mother, Notch. In the example cited it is seen that it was the maternal X that was eliminated. (Fig. 30.)

In the absence of further aberrations in chromosome distribution, all the cells that have their origin in the single X daughter cell will have the 1X : 2A type, and the sex-linked characters of the tissues formed by these latter, if they pertain to parts that do exhibit sex-linked characters, will be those of the parent from whom their X-chromosome was derived. If this is the case, then a gynandromorph of a grade that is compatible with fertility, *i.e.*, one in which the abdomen and genitalia are female, should prove to be

heterozygous in respect of her sex-linked characterisation. This is the case. On the other hand, if the abdomen and genitalia are of the male type in their architecture, the individual should be sterile, since in these parts the sex-chromosome constitution is XO, and it is known from the study of non-disjunction that the XO male in Drosophila is sterile. This is also the case.

If the elimination of the X-chromosome occurs at the first cleavage division of the zygote, the gynandromorphism is lateral; if it occurs at the second, one-quarter of the body will be male in its characterisation. Elimination may occur at any stage of ontogeny and the later it occurs the less will be the area that exhibits male type characterisation. But however large or small this area may be, it will pursue its development under the direction of its own genotypic constitution, and the course of its differentiation is not influenced by the physiological activity of the gonads (as would be the case in the higher vertebrates).

It is to be noted that these mosaic formations are not limited to the sexual phenotype: they are commonly found involving the general phenotype in hybrids. Gynandromorphism results only from such aberrations in the distribution of nuclear chromatin that lead to a sufficient disturbance in the X : A ratio.

Another example of the effects of a disharmony in the distribution of the chromosomes is that furnished by the condition known as balanced intersexuality in Drosophila. In an experiment to determine the locus of a new second chromosome recessive mutant "brown" by means of a back-cross to plexus and speck, one culture produced 96 females, 9 males, and about 80 individuals which were abnormal in their sexual characterisation. These intersexes were large-bodied, coarse-bristled flies with large roughish eyes and scolloped wing margins. The intersexes showed a bimodal variation, one group more closely approaching the female in characterisation, the other the male. All

were infecund. In the female type the genitalia were predominantly or completely female, the abdomen was very much as that of the normal female; spermathecæ were present. The gonads were typically rudimentary ovaries; in many cases the ovarian tissue had a bud of testicular tissue, in others one gonad was a rudimentary testis, the other a rudimentary ovary. Sex-combs were usually present. In the male type, the characterisation of the abdomen and genitalia was predominantly male. Sex-combs were always present. The gonads were typically

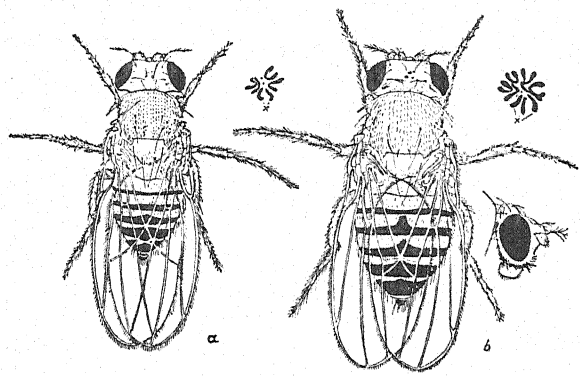


FIG. 31.—The triplo-X female of Drosophila. *a* normal (2X : 2A); *b* (3X : 3A). *After* Morgan.

rudimentary testes, though in a few cases the testes were well developed and contained bundles of sperm.

Moreover, instead of getting but two classes of offspring among the progeny of the back-cross, as would be expected, three classes appeared, plexus speck, plexus brown, and brown speck. This unexpected result can only be explained on the understanding that the mothers had three instead of two II-chromosomes, one carrying plexus brown, one plexus speck, and one brown speck. From their father each had received a II-chromosome carrying plexus, brown, and speck, and from the mothers they had received one of the three kinds of II-chromosome mentioned. She had two genes for each of the recessive characters plexus,

brown and speck, and one for each of the alternative dominants.

Further tests showed that the mothers were also triploid in respect of chromosomes-I and III, whilst chromosome-IV was present either in the duplex or triplex state. It was noticed that these $3N$ (where N = the haploid chromosome number) mothers could be distinguished from the ordinary normal female by their large size, coarse bristles, and rough eyes. That the intersexes were themselves triploid and not diploid with respect to chromosome-II was shown by the

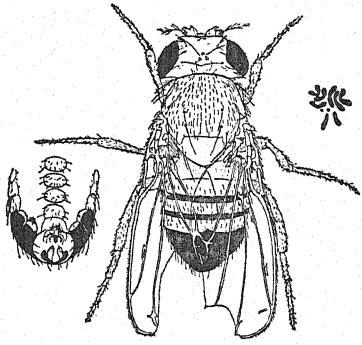


FIG. 32.—Male-type Intersex of Drosophila. (2X : 3A—IV).

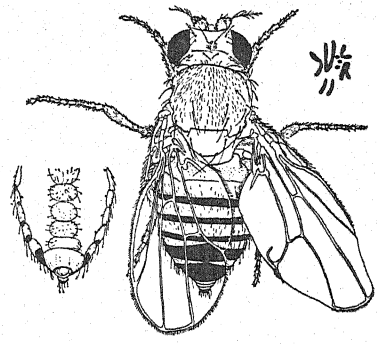


FIG. 33.—Female-type Intersex of Drosophila. (2X : 3A).
After Bridges.

fact that the classes, with respect to plexus, brown, and speck, among them were strikingly different from those in the sexually normal males and females. The intersexes presented three classes also but these were plexus, speck, and brown respectively.

It was readily possible to put this explanation of triploidy to the test of cytological examination and it was found that all the intersexes carried two X-chromosomes, three of each of chromosomes-II and III. Certain of them carried a Y-chromosome and some of them had three IV's, others two. It was found that the triplo-IV's were the female intersexes, the diplo-IV's the male. It is to be noted that the infecund female type of intersex differs from her very

fecund mother in that she is 2X : 3A whereas the mother is 3X : 3A, and that in these intersexes the addition of a fourth chromosome makes all the difference between a male type and a female type.

For the production of these intersexes polyploidy must have occurred in earlier generations. It has been shown that in certain cases ordinary diploid females possess ovaries in which there are areas, the component cells of which are much larger than the normal, and that in these the chromosomes are tetraploid (4*N*). Evidently in some oogonial cell there had been chromosome division of the nucleus so that all mature eggs were diploid. The same process could occur in spermatogenesis.

The following represents the series of sex types in *Drosophila melanogaster*. If the efficiency of the female determining genes (X-borne) is represented as 100 and that of the male determining gene complex in the autosome as 80, a series of sex-indices can be made.

Chromosome Relation.	Sex Types.	Numerical Ratio X (100) : A (80).	Sex Index.	Interval per cent.	X = −6. A = +2.
3X : 2A	Super-female (triplo-X)	1·5 : 1	1·88	50	−14
4X : 4A	4*N* female (normal since ratio X : A is same in all).	1 : 1	1·25	...	−16
3X : 3A	3*N* female	1 : 1	1·25	...	−12
2X : 2A	2*N* female	1 : 1	1·25	...	−8
1X : 1A	1*N* female	1 : 1	1·25	50	−4
2X : 3A	Intersex (female type)	1 : 1·5	0·83	...	−6
2X : 3A (−IV)	Intersex (male type)	1 : 1·5	0·83	33	−6
1X : 2A	Male (normal)	1 : 2	0·63	50	−2
1X : 3A	Super-male (triplo-A)	1 : 3	0·42	...	0

After Bridges.

A review of these facts show that sex-determination is not the function of the sex-chromosomes alone but indicates that the initial sexuality of the zygote is determined by the interaction of the genes resident in the chromosomes, sex-chromosomes and autosomes alike. The addition of more autosomal chromatin (=autosomal-borne genes) to the usual female 2X : 2A balance so disturbs this that the relationship is now that which can be expressed as 2X : 3A and results

in the establishment of a physiological state in which male type characters develop, *i.e.*, the addition transforms a female type of metabolism into one which approaches that characteristic of the male. The addition of more X-chromatin (=X-borne genes) to the usual male 1X : 2A balance so disturbs this that the relationship is now that which can be expressed as 2X : 2A, one that is typical of the female.

There can be no doubt that it is far simpler for purposes of discussion to assume that in the X-chromosomes are genes that are "female-determining," and that on the autosomes

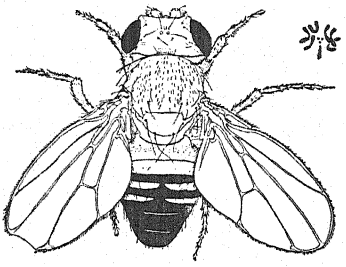


FIG. 34.—Super-male of Drosophila. (1X : 3A).

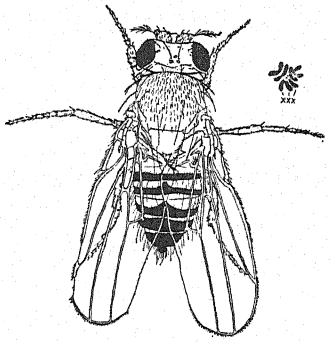


FIG. 35.—Super-female of Drosophila. (3X : 2A).

After Bridges.

are genes that are "male-determining" and that the sexuality of the zygote is determined by the balance between these. For example, if F is taken to represent a set of such female-determining genes on an X-chromosome, if M indicates a set of the male-determining genes in one set (haploid) of the autosomes, and if in their relationship 1F is greater than 1M but less than 2M, then in those classes in which the male is digametic

(FX)(FX)MM is a female because 2F > 2M
(FX)YMM is a male because 1F < 2M

In the classes in which the female is digametic it is necessary to place the male-determining genes on the X and the female-determining genes on the autosomes,

(MX)(MX)FF is a male because 2M > 2F
(MX)YFF is a female because 1M < 2F

and in either case in those circumstances in which the quantitative balance between the male- and the female-determining genes is such as to lead to a situation in which M = F, intersexuality will result. This could be the situation in the ordinary hermaphrodite whilst alternating maleness and femaleness in one and the same individual might be reflections of a change-over in the relative values of F and M.

These formulæ must not be taken too literally: they are but essays in convenient symbolism, and it is to be understood that this is but a way of explaining an imperfectly understood subject concerning which there is a profound lack of physiological knowledge. It would appear to be an accepted fact that in Drosophila the effective factor in the establishment of maleness, femaleness, and intersexuality is the numerical ratio of X-chromosomes to autosomes. Underlying the above explanation is the suggestion that actual differences, to be estimated by differences in the chemical nature of the products of their functioning, undoubtedly must exist in different types of chromatin organisation (genes), and in different gene associations (chromosomes). The chromatin of the X-chromosomes is physiologically different from that in the autosomes, but as yet this difference cannot be defined. At present all that can be stated is that the difference is such that more or less X-chromatin (and also of IV-chromatin) in association with more or less A-chromatin leads to one of three types of internal environment in the zygote and its cells, maleness, femaleness, or intersexuality.

In Drosophila there are sufficient reasons for holding that the Y-chromosome contains no genes that affect sex-determination. It follows then that in the case of the female tissues there are two X-chromosomes in association with two of each of the autosomes, so that if A represents one complete set of autosomes as present in the ripe egg, the quantitative relation, in the body cells of the female, in

the gametes, and in the XX type of zygote, between the chromatin in the sex-chromosomes and that in the autosomes can be expressed by the formula 1X : 1A, whereas in the male somatic cells and immature gametes, and in the XY type of zygote it is expressed by the formula 1X : 2A. In the X-chromosome-bearing sperm the relation is 1X : 1A, in the Y-bearing OX : 1A. The fact that the egg and one kind of sperm are both, in this respect, 1X : 1A, and that the other kind of sperm is OX : 1A, is of interest in that it shows quite conclusively that gamete and zygote are entirely dissimilar in spite of the fact that each may exhibit a similar X : A ratio. In non-disjunction it is common to get an XY-bearing egg which is, in every way, an egg and in no way is an XY individual, a male. That part of the genotype which is concerned in the morphological aspects of sexuality in the zygote is not liberated until egg has been activated by sperm. As will be seen, the genotype of the gamete has no constant relation to the structure of the gamete, for the latter is determined by the kind of organisation of the gonad that manufactured it: an ovary elaborates eggs without reference to their genotype and a testis elaborates sperm without reference to their genotype. A gamete 1X : 1A in genotype will be an egg if it is the elaborated product of an ovary; a sperm if it is elaborated by a testis.

Since it is established that the genes on the X-chromosome are different, as judged by the end-results of their action, from those on the autosomes, and that the chromatin organisation of any chromosome can exhibit change, it follows that chromatin of the X and of the autosomes is different in its organisation and therefore in its physiological activity. Thus the quantitative balance between the X-borne and the autosomal-borne genes differs in male and female tissues, and the physiological states established by the interaction of genes in male and female zygotes respectively will likewise be dissimilar.

It is not necessary—it is probably entirely incorrect, though it is undoubtedly convenient—to postulate male-determining and female-determining genes especially concerned in determining sexuality and elaborating "andrase" and "gynase," the male-differentiating and the female-differentiating substances respectively. Maleness in Drosophila is that physiological state or quality established in a zygote as the result of the action and interaction of all the genes in a genotype that may be symbolised as 1X : 2A. In the beginning maleness in the zygote is a certain kind of internal environment, a certain metabolic level; femaleness is another, and in one or the other organogeny and ontogeny proceed. In the XX type of individual an internal environment of femaleness becomes expressed and the structures that pertain to the sexual organisation will pursue their differentiation under the direction of their own genotype, in the presence of the physiological stimuli exerted by other differentiating and differentiated tissues, and in an external environment which may condition this differentiation. On the other hand, in the XY zygote an initial internal environment of maleness becomes established and the differentiation of the sexual organisation during ontogeny will be such as will yield a typical phenotypic male.

An individual in the case of Drosophila and of the human is a phenotypic male (1) because in the beginning it was a genotypic male (XY); (2) because in this XY zygote the relation between the X-borne and the autosomal-borne genes was such that an internal environment of maleness became established; (3) because in this internal environment the structures concerned in the sexual organisation, being XY in chromosome constitution, developed, and in developing flourished; and (4) because the impress of the external environment did not or could not so affect the developing zygote in such a way as to override the effects of the gene mechanism and to modify the internal environ-

ment based thereupon so that it became physiologically equivalent to the type of internal environment normally associated with the genotype symbolised as XX. For similar reasons the genotypic female becomes a phenotypic female. *Propter secretiones internas totas mulier est quod est*, a female is a female by the totality of her internal secretions, remains true only if it be granted that the phrase internal secretions shall include the metabolic products of her initial genotype.

Sex, physiologically, is an equitable division of labour between two kinds of individuals within a (bisexual) species, one of these being anabolic, the other catabolic, and this difference in the rate and degree of the processes of metabolism is exhibited in every activity of the individual, by the individual cell as well as by the body as a whole. The sex-dimorphic characters are the end-results of the differential development of a common series of anlagen, for sexuality implies the conception of reciprocal differences, maleness and femaleness being but two dissimilar manifestations of a common series of structures and functions.

CHAPTER IV

CONCERNING THE NATURE OF GENETIC ACTION

JUST as, and for the same reasons as, the physicist can speak of electrons and the chemist of atoms, so can the geneticist postulate the existence of his invisible genes. These various conceptions have been constructed out of sufficient numerical and quantitative data. These theories are sufficiently sound to allow numerical and quantitative predictions of a specific kind being made. The gene can be thought of as a unit, as a particular state or organisation of the chromatin in a particular locus in a particular chromosome of a particular species. Its sole properties are those defined by the numerical data elicited through critical experimentation. The correspondence of gene and end-result, the character, is the subject of genetical science; the manner in which the gene is related to the character is not; the phenomena referring to the interval between the gene and the character fall within the field of developmental physiology. However, it can be accepted that all developmental processes follow strictly causal laws, and therefore that if characters are the end-results of developmental processes, and if genes do influence characters, then genes also influence developmental processes. The conception of the gene in no way offends any physical or chemical principle; all that it is required to do is to multiply and to segregate.

It is difficult always to remember that genetics does not teach that each character is the expression of the action of a corresponding single gene, that for each unit character there is a single representative in the germ-plasm. It is

fully recognised that every structure of the body is the end-result of a long series of interacting processes, and that a modification of any step in this series must affect the end-result. The gene is recognised by the end-result and is referred to the particular stage in development when its action was exhibited. If genes produce their effects through the physiological action of their specific contributions to the general economy of the developing zygote, then a mutant gene may lead to such alteration in this state that the development of the whole body is affected slightly and that of a particular organ is profoundly modified. Thus it will appear that a single gene has produced a profound effect upon one organ, though in point of fact all the genes within the genotype will have contributed to this result; the end-result is different because one gene in the whole company had undergone mutation.

The ultimate characterisation of the individual is determined not solely by the genes in their action, for development involves a ceaseless interplay between the individual and its external environment. The absence of an environmental agency essential to normal development will lead to a profound modification of the characterisation of an individual. It is because of this that genetic experimentation must always be conducted under standardised external conditions.

The influence of the environment upon the assumption of a characterisation based upon genes present within the individual can be illustrated by the case of vestigial-wing in Drosophila. If the larvæ of vestigial flies are reared at a temperature of around 31° C., the vestigial condition will not appear, the wings commonly being quite as long as those of the wild-type fly. The expression of this genetic character is conditioned by the environmental factor, temperature.

It is of great interest to note that the effect of temperature upon wing length in Drosophila is remarkably similar to the

effect of temperature on the velocity of chemical reactions. Using the formula $Q_{10} = \left(\frac{K_1}{K_0}\right)^{\frac{10}{T_1 - T_0}}$ for the temperature co-efficient, Q_{10} being the co-efficient of the rate of increase in the reaction for a rise of 10° C., and K_1, K_0 representing constants observed at the temperatures T_1 and T_0 respectively, it is found that the mean Q_{10} derived from data relating to the effects of temperature upon wing length is 1·98. This is somewhat lower than that obtained for a single chemical reaction, but nevertheless it is in striking agreement with the demands of van't Hoff's law.

Eyeless is another character the expression of which is very largely conditioned by non-genetic agencies. In young cultures genetically eyeless flies are eyeless or else have very small eyes; as the culture gets older, more and more of the flies have eyes and the eyes are larger. But if cultures are raised from early or late hatched flies, the results are the same. So also in the case of vestigial, if flies from a vestigial stock reared in high temperatures and therefore having quite long wings are bred, their offspring will be vestigial if these are raised at ordinary temperatures. The gene is not altered though the expression of the character is conditioned. This is also the case with the character abnormal abdomen, in which the regular banding of the abdomen is more or less obliterated. In a culture homozygous for this character, the first flies to hatch, when food is abundant and the atmosphere moist, exhibit the character to a marked degree, whereas later hatched flies, appearing when food is relatively scarce and the atmosphere relatively dry, are much nearer the normal in their characterisation so that the last to appear cannot be distinguished from normal flies. If, however, early hatched flies with markedly abnormal abdomen and later hatched flies with normal abdomen are bred at the same time and under the same conditions, the results obtained in each case are the same, the first to hatch show abnormal

abdomen, the last do not, and this plan of breeding, at least for ten generations, does not lead to any change in this result. These facts are of importance in any discussion concerning the modification of the gene through the impress of environmental agencies. It is seen that they do not support the contention that it is readily possible for an acquired character to be transmitted.

It is seen also that a point mutation, an alteration in the organisation of the chromatin in a single locus, unless balanced by the unmutated state in the identical locus on the other chromosome of the pair, produces a greater modification in the characterisation of the individual than does doubling, trebling, and so on, or halving the number of the chromosomes themselves. Polyploidy and haploidy do not involve the appearance and action of new genes, they result in an increase or decrease in the total number of genes already present in the stock. When the number of chromosomes is multiplied, the individual has the same kind of genes as before and these commonly occur in the same ratio. If the addition or loss of a chromosome or a part of a chromosome disturbs the balance of the genes, some now being present in the triplex or simplex state, the effects are distributed widely among many of the characters. Such disturbance is more profound in forms with relatively few chromosomes, as would be expected, but even in these the effects are small in degree, and widely spread. It is true that a point mutation may, and commonly does, produce but slight and widespread effects though usually it is the case that, in particular, one organ or part is modified to a striking extent.

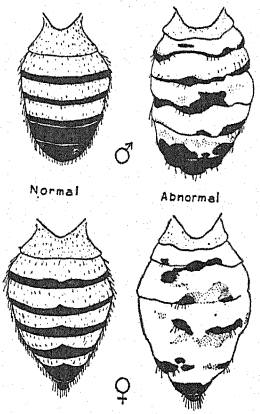


FIG. 36.—Abnormal abdomen in *Drosophila melanogaster*. *After* Morgan.

The most convincing argument in favour of a specific action of each gene is to be found in the case of a series of multiple allelomorphs. These must be distinguished from multiple factors which are genes, producing separately the same effect and in combination yielding a cumulative or summative effect. A multiple allelomorphic series can be illustrated by the sex-linked eye-colour of Drosophila. White-eye is a recessive character associated with a particular state of the chromatin in a locus 1·5 morgans from yellow on chromosome-I. It is allelomorphic to red, giving a 3 : 1 ratio in F_2. In a white-eyed culture another eye-colour, eosin, appeared. Eosin and red are allelomorphs, giving a 3 : 1 ratio in F_2 just as did white and red. The C.O.V. of eosin and yellow is 1·5 as is also that of white and yellow. Other eye colours appeared later in different Drosophila cultures, cherry, tinged, buff, ecru, apricot, ivory, coral, and blood. Each of these is allelomorphic to red and its C.O.V. with yellow is 1·5. A mating between any two of them (including eosin and white) yields females with eye colours which are a blend of the two parental colours and males with the eye colour of one or of the other parent, for example, cherry eye ♀ × white ♂ = cherry-white ♀♀ and cherry ♂♂. This sex-difference is due to the fact that the female has two X-chromosomes and that the F_1 female is heterozygous for her sex-linked characters.

The genes for each of these characters must necessarily be resident in the same locus 1·5 morgans from yellow in chromosome-I. They represent different states of the same chromatin and each state is stable and specific. Though the gene is stable, mutation can and does occur, and so it is that just as eosin appeared in a white-eyed culture, so a return mutation can yield a white-eyed individual in an eosin-eyed culture. Mutation is rare, but it is commoner in some loci than in others for reasons that are not yet understood. It may be *gametic*, occurring prior to the maturation of the gamete when, unless the chromosome

concerned passes into a polar body, its effects may be profound and patent upon the entire development of the individual. Being gametic it can enter the zygote from one parent only, and if it is a recessive mutation, the corresponding character will not appear until some subsequent generation in which two individuals, each simplex in respect of it, chance to mate. If it is a dominant, then the character will appear in the immediate offspring. The mutation may be *zygotic*, occurring immediately after fertilisation, and its effects will be exhibited by the individual during the course of development. It may be *somatic*, occurring in one cell of the developing individual. All tissues arising from such a cell will exhibit the mutant character, but the germ cells will not be affected and the condition will not be inherited.

It is true that the present-day knowledge of organic inheritance is founded on the hereditary behaviour of characters many of which may be regarded as pathological. Nevertheless, in tracing the inheritance of abnormality the mode of inheritance of normality has been disclosed. Opposed to each defect-producing gene there is a normal partner, its allelomorph, and one of these cannot be studied without the other. There are many characters which, though they are unusual, cannot be labelled as harmful.

It is not uncommon to find in the case of Drosophila that the duplex state of a recessive gene produces a lethal effect, leads to the development of a condition of such a kind that the further existence of the individual is made impossible. As an example of a lethal characterisation, the case of the homozygous yellow mouse may be cited. Yellow mice produce smaller litters than do mice of other colours, and on the average their litters include 2 yellows and 1 grey in every 3. Yellows do not breed true and their mating always yields a proportion of greys; they are always heterozygous yellows. The ratio 2 yellow : 1 grey suggests that actually a 3 : 1 ratio is involved and that the homozygous yellow is missing. This would indeed seem to

be the true explanation: the homozygous yellow perishes *in utero* at too early a stage to permit the cause of death to be diagnosed. In the heterozygous yellow mouse, the lethal gene is in the simplex state and is balanced since the character is an autosomal one and not sex-linked. In the case of a sex-linked lethal the monogametic sex (XX) can, of course, have this lethal balanced since she has two X-chromosomes to carry the allelomorphic genes, lethal and normality. The digametic male, however, either has the lethal gene in his X, or he has not; either he dies or

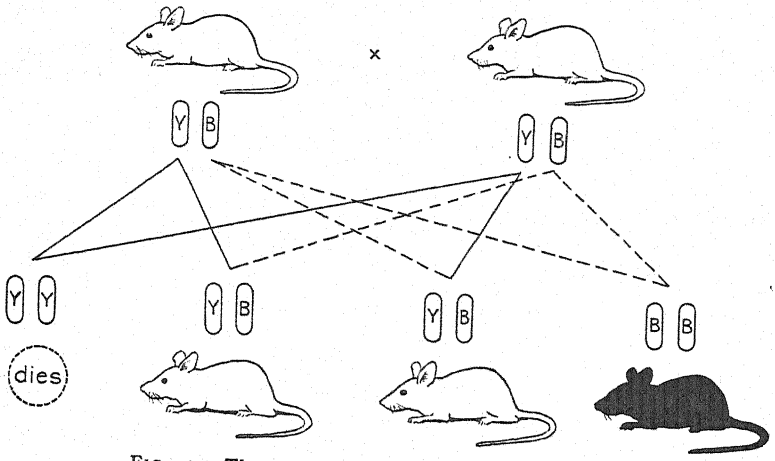


FIG. 37.—The case of the homozygous yellow mouse.

he is entirely normal. Through the action of such a recessive sex-linked lethal, therefore, the sex-ratio of a generation can be profoundly altered.

For example, there is a lethal, called lethal III, 26·5 morgans from yellow on chromosome-I of Drosophila. If a white-eyed female, simplex for lethal III (1_3), is mated to a normal male (red-eyed and without this lethal) all the daughters will be red-eyed but half of them carry lethal III in the simplex state and the other half will be normal, whilst only one half of the sons will survive. If one of these is mated with one of his sisters carrying the lethal in the simplex state, an F_2 including 4 red ♀♀, 3 red ♂♂,

4 white ♀♀, and 1 white ♂, *i.e.*, 7 reds : 5 whites in every 12 and 2 females to 1 male in every 3. These unusual ratios indicate the presence of a single sex-linked recessive gene.

If the following symbols are used, the results can be illustrated. w = gene for white eye; W = gene for its allelomorphic red-eye; l_3 = gene for lethal; L_3 = gene for its normal allelomorph. X and Y = sex-chromosomes: ( ) = genes on the included X.

$(wl_3X)(wL_3X)$	×	$(WL_3X)Y$		P_1
$(wl_3X)(WL_3X)$	$(wl_3X)Y$	$(wL_3X)(WL_3X)$	$(wL_3X)Y$	F_1
Red simplex ♀	dies	Red ♀	White ♂	

In the formation of the gametes of the female simplex for l_3, there will be 25 per cent. crossing-over between the loci w, l_3, and W, L_3, so that she will produce four types of ova in the following proportions:—

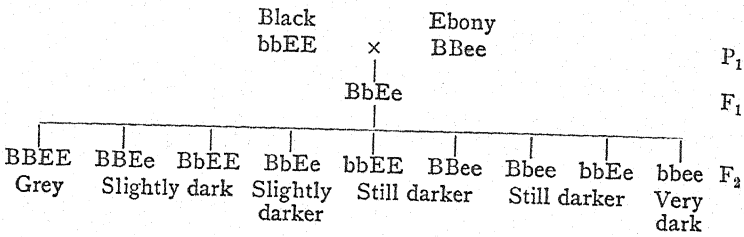
Zygotes.	Sperm.	Ova.	Sperm.	Zygotes.	
3 $(wL_3X)(wl_3X)$		3 wl_3X		$(wl_3X)Y$	3 ♂♂ die
3 $(wL_3X)(WL_3X)$		3 WL_3X		$(WL_3X)Y$	3
	wL_3X		Y		
1 $(wL_3X)(wL_3X)$		1 wL_3X		$(wL_3X)Y$	1
1 $(wL_3X)(Wl_3X)$		1 Wl_3X		$(Wl_3X)Y$	1 ♂ dies

or 4 ♂♂ to 8 ♀♀ in every 12. 7 reds to 5 whites in every 12. 1 white to 4 white ♀♀ in every 5 whites and 3 red ♂♂ to 4 red ♀♀ in every 7 reds.

The F_1 males mated to their sisters without this lethal gene beget equal numbers of reds and whites and of males and females, a result which is in every way unexceptional.

There are genes which produce effects that are so similar as to be indistinguishable and it is only through controlled breeding experimentation that their independence can be demonstrated. For example, the recessive characters black and ebony body-colours are very similar, yet their genes are quite distinct, indeed they reside in different chromosomes. Black mated to ebony yields an F_1 slightly darker than either parental form and in F_2 there appears a graded series

of body-colours, ranging from very dark individuals to individuals coloured as the wild type. Dominance is not complete in the relation black - ebony and each colour class, each in its own mode overlaps its neighbours. These results can be illustrated by means of the conventional symbols (e = gene for ebony, b = gene for black).



This result is similar to that of multiple factors, independent genes producing similar results and exhibiting in combination a cumulative effect.

A small variability in F_1 and a greater variability in F_2 indicates the presence and action of many genes producing similar or apparently similar effects. This applies particularly to the case of quantitative characters such as size and length.

There are genes which in their action produce the agouti pattern upon the hair of the mouse and of other animals, an instance of cellular differentiation repeating itself rhythmically, there are others which produce bifurcation of bristles, an instance of dichotomy, and yet others which produce incisions in the insect's wing, an effect similar to the lobulation of an organ. There are genes which govern the formation of the tracery on the butterfly's wing and the piebalding of the horse's coat: there are others which determine the kind of metabolism exhibited by the individual, as in alkaptonuria, for example. All these characters are of the same order as the whole of the events of development between its inception and its end, and this being so, it is not unreasonable to assume that the events of development are themselves controlled by genes.

It is commonly accepted that there are indeed genes that correspond to the individual and racial characters, but it has been argued that though there may be genes for human eye-colour, no genes for humanness itself have ever been discovered. It certainly is true that as yet no experimentation which could be expected to reveal such genes has been undertaken. But since it is established that all the genes within a genotype do not come into action synchronously, and moreover that certain genes actually exert their action in the gamete before fertilisation, it is not impossible to think of the genes for the specific characters exerting their influences in the gametes and converting a previously non-specific gamete into a human gamete. Such a conception involves the suggestion that, if it were possible to replace the chromosome complex of a gamete of one species sufficiently early in gametogenesis by that of another species, the gamete would then become specific for the characters of the form to which the implanted chromosome complex belonged.

Though it is true that a purely numerical treatment of the observed data that emerge from breeding experiments is adequate to disclose their genetic basis, it is difficult for the geneticist to avoid the excitement of embarking on speculations concerning the physiological processes which undoubtedly underlie such phenomena: it is difficult for one perhaps qualified for genetical experimentation to remind himself that he is not also equipped with sufficient physiological knowledge to ensure that his adventures in this latter field shall not be a source of danger to his own subject. As long ago as 1903, it was first suggested that the self-perpetuating entities we now know as genes were of the nature of enzymes, and since that time it has often been assumed that genetic differences in characterisation were to be interpreted as the results of different chemical processes. More recently the conception of the chemical nature of the gene has been influenced by developments in physical chemistry, particularly those relating to van't Hoff's

discovery that most chemical reactions are increased in rate three or four-fold by a rise of 10° C., and by his suggestion that similar relations might hold in the development and growth of living things. It was quickly shown that in general this was so, and soon it was suggested that each cell nucleus was a centre of autocatalytic changes and later that there were genes determining the rate of cell division and that these genes could be thought of as definite quantities of ferments. Not only has this theory been applied to the problems of growth of the individual as a whole, but it has been applied also to the chromosomes themselves. At each cell division each chromosome (and by implication each gene resident within it) divides, and each then grows to its former size. The amount of chromatin thus becomes doubled at each cell-division. This increase proceeds in a geometrical series and gives an exponential curve which indicates that the process is of such a kind that it becomes more and more accelerated for the reason that more and more chromatin becomes available as cell-division succeeds cell-division. The process does indeed closely resemble the first part of an autocatalytic curve. After a time the division rate slows down and so the later part of the curve comes to resemble the second part of the autocatalytic curve.

It will be remembered that in extra-cellular autocatalytic reactions in which enzymes are involved the enzyme itself does not increase in amount and one of the products of the reaction is the autocatalyst. It does not seem probable that the genes themselves are enzymes, but it is not improbable that the genes are protein bodies one of the activities of which is that of producing enzymes which, being present in each cell of the body, take part in catalytic reactions in the cytoplasm.

Manifestly it is too early to discuss at all profitably the ultimate nature of genetic action in terms accurately physiological. But this must and will be done when more is known.

CHAPTER V

CONCERNING CONSANGUINITY IN MATINGS

ENDOGAMY is that system of breeding in which closely related individuals are interbred. In *inbreeding* the closest possible types of mating are practised, sire to daughter, mother to son, brother to sister; in *line-breeding* the matings are between individuals within one line of descent, excluding those which would constitute inbreeding. In this discussion, the term inbreeding will be used loosely to include both in- and line-breeding. Exogamy is that system of mating in which the individuals are unrelated. Since all animals and plants of the same breed and variety are necessarily related in some degree, the terms inbreeding and outbreeding are relative. Inbreeding merely implies that the individuals concerned possess fewer different ancestors in some particular generation or generations than the maximum possible number for that generation or generations.

Inbreeding has been deliberately employed by animal breeders for two hundred years or more: it is the sole method of reproduction of many naturally self-fertilised plants: it has been practised in the human race, *e.g.*, in the royal families of Egypt, and to a lesser extent and degree among the royal families of Europe. The records of the breeds of domesticated animals show that close inbreeding of sound stock, if associated with intelligent elimination of the weakly and abnormal, can be practised for many generations without any undesirable consequences. They show, in fact, that some degree of "narrow" breeding is essential for progressive and permanent improvement leading to the production of a uniform and true-breeding stock. They also

show that inbreeding has been and can be a particularly dangerous tool in the hands of the breeder, for there are many instances of disappointing regression, of diminished vigour, lowered powers of resistance, decreased fertility, and of reduction in size among inbred stock. The evidence concerning the results of inbreeding is conflicting, and the breeder and sociologist, playing for safety, have commonly avoided this system of mating. Breeders generally are very disinclined to run the risk of practising inbreeding because the disastrous results of this system of mating are more clearly remembered and are more common than are the successful. In human society there are customs and laws which forbid or discourage marriages between relatives.

But though the facts may vary, there has developed among geneticists a considerable degree of unanimity concerning the principles involved, and a general interpretation has now been proposed which explains the conflicting results in genetical terms. This has emerged from the results of carefully controlled experimentation and the critical analysis of the data thus obtained.

The earlier experiments on inbreeding with the usual laboratory material (rats, mice, guinea-pigs) gave results which appeared to confirm the opinion that inbreeding necessarily involved lowered fertility and vigour and increase in abnormalities, mortality, and proneness to disease. But the more recent and much more extensive experimentation has revealed the faults in the previous work and has furnished satisfactory explanations of the deleterious results showing that these must not be ascribed to the system of mating employed but to other causes.

Rats have been bred, brother to sister, for twenty-five generations, and it has been demonstrated that such close inbreeding, if accompanied by the most rigorous selection, does not necessarily produce any adverse effects. Twenty-three generations of the closest inbreeding, and involving about 30,000 guinea-pigs, revealed that the average effect

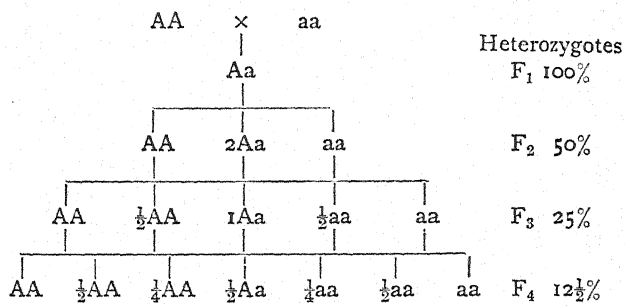
of inbreeding was the production of a decline in all elements of vigour. The mortality at birth and before weaning, the growth rate, the litter size, fertility, disease-resistance, were all adversely affected. This decline in general physiological fitness, which occurred also in the case of the rats referred to above, was an average result, but it occurred in different families within the inbred stock. The method of experimentation is that of taking the offspring of a single mating and of dividing these into pairs which then become the original pairs of different lines. In each generation a brother and a sister are mated and the lines are never allowed to become mixed. If such a method is adopted, it will be found that most of the lines, in the majority of cases, will quickly become extinct, but that one or two will compare very favourably indeed with the original stock.

In plants and in animals there is a progressive decrease in size and performance during the first few generations of inbreeding. After seven generations or so, however, the inbred lines become stable and thereafter the decrease is negligible. Among the different lines within an inbred stock there quickly appear characters which distinguish line from line. As inbreeding continues, these line-characters become fixed in each line, and shortly thereafter variation within the line is no longer noticeable. Many of the lines are characterised by profound defects of one kind or another, but a few of them are notable for their stability and healthiness even though they are not as vigorous generally as the original parents.

Inbreeding produces two principal effects: (1) a reduction in the variability in the expression of inherited characters within inbred lines or families so that members of such families come to resemble each other more and more closely and to differ from individuals of other lines more and more sharply, and (2) a usual but not inevitable decline in general vigour.

The chief effect of inbreeding expressed in genetical terms is the isolation of homozygous types, to increase the

proportion of factors in the duplex state and to decrease the proportion of factors in the simplex state in the genotype of individuals within a population. This effect can be seen in the case of a self-fertilising plant, an F_1 heterozygous for a single character.



This is manifestly a geometrical series, and the percentage of heterozygous forms in the 8th generation will be $100\left(\frac{1}{2}\right)^{8-1} = \frac{100}{128}$ or less than 1 per cent. The proportion of the heterozygous Aa class is steadily reduced by its breaking up into AA and aa types, and the proportion of the homozygous types is reinforced since these remain homozygous and breed true when once formed. This reduction in heterozygosity proceeds automatically in the case of all factor pairs involved and the rate of reduction of heterozygosity depends on the degree of inbreeding that is practised. It is most rapid under self-fertilisation, less rapid in the case of brother × sister matings, and does not take place at all when second cousins are continuously mated generation after generation. Theoretically, complete homozygosity should be attained in the 10th generation of self-fertilisation: in the case of continued brother to sister matings starting with heterozygotes, the proportion of heterozygotes should be reduced from 50 per cent. to 5 in this time. Of course, such theoretical expectation is not realised in practice, for breeding is seldom at random as required by theory.

The relation between this factorial interpretation and the observed effects of inbreeding upon vigour is that recessive characters are more frequently harmful than beneficial to the individual. In a heterozygous population these characters are not expressed, the factor for a recessive character being dominated or balanced by its allelomorph. Inbreeding results in the segregation of recessive factors, individuals duplex for such factors appear and the recessive characters, commonly deleterious, frequently lethal, are exhibited by an increasing proportion of the population. The differentiation among inbred families which takes place under inbreeding is the result of the chance segregation of certain groups of factors into a given line and of the subsequent stabilisation of the characterisation through increasing homozygosity.

It follows then that if the deleterious results of inbreeding are to be ascribed to the isolation of types homozygous for characterisations which are harmful to their exhibitors, and if such characterisations are but the expression of genetic factors or genes, these genes must be present in the hereditary constitution of the individuals with which the practice of inbreeding was started. The effects do not depend on any pernicious attribute of the system of breeding: they are the reflection of the genetic constituents of the individuals concerned. Consanguinity itself is no bar to mating. If inbreeding results in disappointment, all that has happened is that that which previously was hidden in a heterozygous stock has now been brought to the surface. Inbreeding is only disastrous if the ingredients of disaster are already in the stock. Inbreeding will purify a stock but the process may be most expensive. The relative freedom of individuals of inbred stocks from inherent defects is due in many cases to chance, but in others it is the result of antecedent inbreeding which eliminated the harmful recessives.

To the breeder the geneticist can say, "If in your stock

there are no hidden recessive factors for undesirable qualities, then you need not fear inbreeding, for this is the surest and quickest method of fixing the desirable qualities which your stock now exhibits; but if such recessive factors are present, then you must expect trouble." To the question as to how the breeder may know whether or not such recessive factors exist, the geneticist can but ask that he may be shown full and accurate pedigrees of the individuals and families concerned. Sometimes these are useful: commonly they are not, for the reason that herd book records are neither full nor accurate. A study of the progeny of an individual is more helpful than is that of its ancestry. So also in the case of the human, consanguinity in marriage is not dangerous in itself; it is dangerous for the reason that human stocks are loaded with undesirable recessives, hidden in heterozygosis, which are revealed when closely related individuals marry. The results depend on the existence of many hereditary factors affecting development; many of them, recessives, affecting the organism adversely, on the distribution of these factors in a population, and on the segregation and expression of these factors as directed by a particular system of mating. Inbreeding exerts its effects solely through the medium of inheritance and not through the blood-relationship of the individuals concerned. In the human it can be accepted that each individual is heterozygous for a large number of his or her characters and that this heterozygosity is maintained by the continued out-breeding. If, however, individuals similarly heterozygous mate, there is the chance for the automatic isolation of homozygous combinations. Factors for deleterious characters meet to reinforce each other, recessives become extracted, and the extracted recessive is often the undesirable.

Genetics, in this matter, is on the side of the big battalions. The smaller the population which is ring-fenced by any kind of barrier to marriage with outside stocks, the greater is the danger of degeneracy through inbreeding.

It follows, then, that not only are the hereditary factors corresponding to undesirable characters sorted out to form combinations leading to sterility, deformity, and derangement, but that stocks exposed to inbreeding can become homozygous for characters that are definitely desirable through the workings of the same mechanism. If inbreeding exposes the undesirable, it equally thoroughly emphasises the desirable, and the desirable will breed true when complete homozygosis in respect of these characters is attained. Any selection for improvement in characterisation through breeding must be without avail when for all its characters a stock is homozygous. Any variation that exists in such a stock is due to differences in experience. It is a simple matter to produce modification in the average characterisation of a heterozygous stock by selection of the parents of each successive generation. Improvement in such circumstances merely implies the replacement of heterozygosis by homozygosis. But selection with a homozygous stock is unavailing since for genetic reasons such stock must necessarily breed true to its own characterisation, and any modification of such a characterisation must be brought about by the impress of environmental agencies.

The reasons given above will show how it is that many pathological conditions appear in the offspring of matings of near relatives more commonly than among the children of unrelated individuals. It is because many such conditions are recessive characters and the marriage involves the bringing together of two individuals each carrying the factor for such a character in the simplex state. If between normality and abnormality in this case there exists but a single factor difference, the chances of an extracted recessive appearing are as 1 : 3.

In assessing the results of inbreeding in the case of the human, it must not be forgotten that incest, *i.e.*, inbreeding in the narrow sense of the word, is much more common in those classes of society which for other and sound reasons are

regarded not only as socially but also as genetically inferior. That the offspring of an uncontrolled father and his feeble-minded daughter should be socially, physiologically, and psychically unworthy is not an indication that incest itself is pernicious but that it should be forbidden in the case of unsound stock. Incest is not of common occurrence among responsible individuals living in communities in which such a practice is held to be abhorrent or unlawful. This is as it should be, since there is good reason to hold that such a practice would reveal many of the recessive and adverse characters inherent in human stocks. However, it would seem to be a fact, sufficiently secure for the foundation of sociological practice, that incest between individuals of undoubtedly sound stock, already homozygous for many desirable characters and simplex in respect of factors for no harmful recessive characters, is a sound biological proposition. But before there can be any kind of advocacy for this practice on biological grounds, there must be full and accurate knowledge of the hereditary constitutions of the individuals concerned. Until then no biologist can be prepared to oppose seriously the conventional attitude towards this subject.

There is no genetical support for any objection to the marriage of individuals no more closely related than is a man to his deceased wife's sister. There is, however, for the common anxiety concerning the result of the marriage of first cousins. If in the pedigree of either or both there are examples of undesirable characters, then such a marriage can be provocative of the appearance of these characters among their offspring. If, however, nothing but good, physically, physiologically, and psychically, is revealed by their pedigrees, cousinship cannot be used as a barrier to their mating. These remarks apply not only to the case of cousins. They hold also and equally in the case of the marriage of individuals of two unrelated stocks which in their pedigrees show similar records of undesirable characters.

It is not for the biologist, as biologist, to discuss the question of marriage without children in cases in which parentage is undesirable for reasons of organic inheritance. This problem is not for the general biologist alone, and thus far the science of the biology of the human is in its infancy.

Before leaving this discussion on inbreeding, it will be convenient to refer to a matter which, though it has no relation to this subject, can most conveniently be discussed at this point. It is the frequency of mating among individuals who are, or have been, living temporarily in one kind of institution or another. Residency in almshouses, asylums, sanatoria, in which the segregation of the sexes is imperfect, commonly leads to the mating of like with like. Pauper mates with pauper, being unattractive to the civically worthy, deaf-mute marries one like unto himself, so that he may have companionship in his dreadful isolation; in fact, it may be said that deaf-mute must marry deaf-mute or else remain celibate. Such companionship in marriage is not to be condemned, but if it leads to the production of pauper children or to any increase of deaf-mutism among the population, it surely ought to be prevented.

It has long been recognised that crosses between different strains, varieties, or races of animals and plants frequently, but not invariably, lead to the production of progeny more vigorous than either parental stock. To such manifestations of hybrid vigour the name heterosis, at once descriptive and explanatory, is given. Heterosis is the reverse of the diminished vigour that frequently follows upon inbreeding and it is to be explained through an appeal to the same mechanism. Heterosis is most marked in the F_1 generation produced by the mating of individuals from different but inbred lines, and if inbreeding is thereafter practised, this vigour gradually but surely diminishes with each succeeding generation. The genetic interpretation of heterosis rests on the same assumption as was used in the case of the results

of inbreeding. Inbred lines possess in their hereditary constitutions factors which affect such physiological characters as growth rate, rate of development of sexual maturity, fecundity, and such like. Different inbred lines have come to possess different hereditary constitutions through segregation, isolation, and fixation by inbreeding. If then the factors that make for general vigour are cumulative, those received by a hybrid between two inbred lines from one parental stock being reinforced by those received from the other, then hybridity will imply heterosis. It is the pooling of the favourable genes that makes for increased vigour.

Again, it is necessary to point out that outcrossing is in itself not primarily responsible for the results that emerge from its employment. It creates nothing, no more than does inbreeding. The effects of outcrossing depend upon the hereditary contributions of the two parental stocks. If each contributes to the hybrid offspring factors in respect of physiological characters which amplify and emphasise the action of factors of a similar kind, though actually different, received from the other, then heterosis will result. All outcrosses cannot be expected to yield advance upon the parental types: such are not complementary or compensatory in the matter of factors for desirable characters must be provocative of disappointing if not of disastrous results.

It is impossible on purely genetical grounds to advocate or to condemn all interracial marriages. These involve racial, group, family, and individual characters. In respect of individual characters there is no reason why two people of different biological races should be more alike or unlike than two people of one and the same race. So also in the case of family and group characters. It is possible to secure as considerable heterosis or, on the other hand, decline of vigour through marriage of individuals within the same race as in marriage between individuals of different races. It would seem reasonable to expect better results from the mating of individuals of different northern European

stocks than from that of individuals of differently coloured races or of Nordic and Alpine or Mediterranean respectively. But it is really impossible to generalise, for marriage is a combination of individuals not necessarily or completely representative of the races to which they belong. Races are not genetically homogeneous. In this matter it is commonly impossible to disentangle the biological from the social aspects of interracial marriages and until this has been done it is impossible to assess at all accurately the biological advantages or disadvantages of such marriages. The Eurasian, for example, may be a biological blunder, but this cannot be proven until the social disadvantages of being a Eurasian have been removed. Before there can be any advocacy or condemnation of such interracial mingling, it is necessary to possess a fairly complete genetical analysis of the races concerned. This is best achieved through controlled experimentation. History would seem to show that there is no really serious biological objections to racial hybridisation and that the widespread repugnance to it has been born of political and religious sentiment and prejudice and nurtured by the barriers of physiography, languages, and social customs. Difference is too commonly interpreted in terms of superiority and inferiority. Such as are different are regarded as inferior, and marriage with an inferior is condemned. The argument is simple but not necessarily sound. It is the Nordic who holds that the Nordic is genetically superior: the Alpines and the Mediterraneans cannot be expected to subscribe to this contention: they will agree that the Nordic is different and thank their gods that this is so.

Marriage biologically is an individual not a racial affair. Mates are attracted to each other, or else marriage is a matter of convenience. If an individual is incapable of responding to a biologically worthy attraction, then he is socially unworthy and is treated as such. Racial hybridity should not be assessed from an incomplete examination of

the results of the casual intercourse of irresponsible individuals or of the half-breeds produced by individuals of socially and genetically inferior stocks of two races, these not being fair samples of a racial hybrid population. It is commonly and easily stated that the half-cast inherits the vices of both parental stocks and the virtues of neither. But this is loose thinking, for it has not yet been shown that qualities of this kind are genetic in their basis. The half-breed may be vicious, judged by the standards of either parental stock, but this viciousness may be but the reflection of his peculiar social inheritance, and this is most readily modified if such modification is attempted through reasonable appeals to the emotion of an idealism. So long as a half-cast remains an outcast, so long must he be non-social.

If there are genetically superior and inferior races, and if races are judged according to their performance in relation to a common standard there cannot be much doubt that there are, then since the usual result of such interracial mating is the production of a generation intermediate in its characterisation, interracial marriages cannot be condemned on biological grounds, for if the hybrid is inferior to one parental stock, it is superior to the other. If the hybrid replaces the inferior stock, and if the average of the hybrid is definitely superior to that of the stock which it displaces, then surely its production must be regarded as a gain. This is a purely biological opinion that cannot be expected to modify social attitudes. However, since there are interracial matings, such as the Maori × Anglo-Saxon or the Amerind × Anglo-Saxon, to which no social prejudice is opposed, it may be helpful to note that in such cases the social sanction is not opposed by biological theory.

The problem of interracial marriages only begins with the production of the hybrid stock, however. The more serious difficulties are encountered when the hybrids interbreed and back-cross, for then segregation and recombination

operate, and a variety of different character classes is liberated. The problem of interracial marriages is not that which concerns the marriage of the original parents of the hybrid stock, but is that of the hybrids themselves. Races can differ in respect of so great a multitude of hereditary factors that in the second hybrid generation and thereafter there is to be expected a veritable epidemic of variants. This in itself is sufficient to render many interracial mixtures undesirable.

There is no point in contemplating the breeding of a new race type by deliberate racial hybridisation and subsequent selection until it has been shown conclusively that the present stocks of relatively pure races are, for genetic reasons, unfitted for the destiny which mankind has arranged, or should be arranging, for itself. A new breed of domesticated animals is evolved for the definite purpose of fitting into a set of environmental circumstances which can be defined in advance. The new type is deliberately fashioned so that its equipment is that demanded by its intended destiny. But what is the future evolution of mankind? It will surely take the form of the deliberate and conscious manipulation of mankind by man. Man must produce descendants that will be genetically equipped to reap to the full the greater opportunities of an environment created by man. It is not known yet what the future environment is to be; or, on the other hand, what is to be the standard of improved humanity: until these are known, it is premature to think of breeding a special type of man. And in any case, there is so much variability within the pure stocks already existing that there is no reason to think that anything more than careful selection among these stocks will ever be required.

CHAPTER VI

INHERITANCE IN MAN

1. *Normality*

IN the beginning of the geneticist's analysis of the human, a totally inconvenient and most unsatisfactory experimental material, it is indeed necessary for the biologist to deal with such characters the definition of which is simple and the mode of inheritance of which may be expected to be relatively straightforward. If it can be demonstrated through the use of glaringly obvious characters that there is a mechanism in the human precisely similar to that which in the extensively used forms has been shown to accommodate all the demands made upon it by the varied facts of organic inheritance, then one is justified in holding the view that this mechanism will ultimately be shown to be capable of accommodating the more complicated varieties of hereditary transmission of the more complex, and presently unanalysed, human characters concerning which to-day little or nothing is known. Until such a mechanism has been stretched beyond its breaking point, there is no call to postulate the existence of a hereditary mechanism in man that differs widely from that which has been amply demonstrated in the case of other forms.

As yet there is but little knowledge of the genetic basis of humanness and very little of those genetic differences that distinguish the races of mankind. That racial characters are inherited is beyond all doubt, but their analysis is difficult because they are seldom of the alternative type but commonly differ only in degree and because through con-

tinued crossing the present races are largely heterogeneous and variable. There is no single standard of normality with which an off-type may be contrasted, and this fact constitutes a very real difficulty in genetical analysis. From the little that is known, however, we are permitted to assume that racial differences are based upon the action of a very few hereditary factors, and that as far as the great majority of hereditary factors are concerned, all races are exactly alike. The fact that racial differences are truly inherited is important both theoretically and practically, but for the reasons just stated a study of them has added but little to our knowledge of human inheritance, and in order to gain precise and definite information concerning the genetical behaviour of human characteristics, the inheritance of differences between individuals of the same racial stock must be studied and the transmission of single, clearly recognisable, characters must be traced.

Physical and physiological characters are more easily followed in inheritance than the mental, for the reason that they can be more readily recognised and measured. It is for this reason that more is known concerning them. For the same reason more is known concerning the hereditary transmission of anatomical defects and of physiological derangements than of that of normal characters. Because of this, the complaint is sometimes made that the present-day knowledge of human inheritance is nothing but a compilation of cases of the probable transmission of human defects and that in most projects for racial improvement the greatest stress is laid upon efforts to eradicate these. The fact is that thus far it is easier to speak more confidently of the inheritance of defects than of that of normality.

Investigation has shown that in their hereditary behaviour these glaringly obvious and easily followed characters are exactly equivalent to instances of inheritance which have been demonstrated in animals and plants, the genetics and cytology of which are very completely known. This being

so, it is reasonable to assume that in the human there is a mechanism of inheritance exactly similar to that which is found in more thoroughly and critically studied forms. Simple dominance, simple recessivity, multiple allelomorphs, and sex-linkage have been amply demonstrated. A number of characters have been shown to be based on two or more pairs of multiple factors and to exhibit, therefore, that blending type of inheritance which is so common in the case of all quantitative characters. Most of the different size characters of the body seem to exhibit this form of inheritance and their study is of the most profound importance since there are many cogent reasons for thinking that certain types of bodily conformation are closely, if not inherently, associated with certain susceptibilities towards disease. But size is a growth phenomenon and depends, among other things, upon the time at which increase in the length of the bones ceases, this in turn is connected with the time of attainment of sexual maturity, and this depends on the time of functioning or on the amount of secretion of the different endocrine glands. These interrelationships make the study of bodily configuration a matter of very considerable difficulty. However, there is nothing in these complications that precludes the possibility that the ultimate source of differences of this kind is to be found in the action of genetic factors.

But more important than the physical and physiological characters of an individual under the conditions of modern social organisation are his psychological qualities. The physician and the surgeon can correct bodily abnormalities: the educationalist and the psychologist are faced with a far more difficult task.

A definite solution of the problems of the inheritance of the mental qualities of the human is a matter of very serious difficulty. In the case of the experimental animals, through the use of which the geneticist developed his techniques, the analysis of the mental characters cannot

readily and exactly be investigated. Such characters in the human cannot be easily defined and assessed. Moreover, it is certain that many mental qualities especially when estimated by casual observation will be more reflective of the nurture of the individual than of his organic inheritance.

Up to the present time such vague qualities as mental capacity, immorality, and patience, have been studied and have been regarded as being either present or absent according to some subjective estimate which is commonly obtained at second or third hand. It has then been assumed that the assigned differences are mainly genetic in origin and pedigrees have been combed in order to trace the mode of their inheritance. Manifestly, this method of approach is most unsatisfactory. As is the case in the matter of the physical characters, most attention has been paid to abnormal conditions which in their behaviour point to the existence of a mechanism.

Feeble-mindedness is an oft-quoted instance of a typical recessive character, but until this condition can be defined exactly, until it has been shown what acquired physical aberrations may lead to its development, it cannot be finally accepted that there is a single factor difference between feeble-mindedness and normality, whatever these may be. Pedigrees that furnish a continuous series of non-social individuals do not necessarily mean that something organic is being inherited: it is quite possible that if a group of individuals of potentially average mental ability are living under demoralising social conditions, one or more will be overwhelmed. If the conditions are continued, then the influence of those who succumb can be communicated and not transmitted to the next generation.

There is no doubt, however, that many abnormal mental states appear, and strongly appear, to be inherited. But this is not enough, there must be no doubt upon the matter before sociological endeavour is built as a superstructure upon genetic theory. So long as the physiological back-

ground of these abnormal mental conditions and the external agencies which are contributory to their development remain obscure, it is impossible to arrive at a satisfactory knowledge of their genetic basis.

If it is not yet possible to speak with confidence concerning the mode of inheritance of these easily recognisable and readily traced abnormal characters, it cannot prove very profitable to discuss the many claims that have been put forward concerning the inheritance of normal psychological characters. It is enough to say that as yet we know nothing at all definite concerning them, and that it is of the greatest importance that their investigation shall be ardently prosecuted.

To the educationalist, and to the sociologist also, one of the most important problems in inheritance is that which is concerned with the transmission from one generation to another of educability, of the capacity for mental development, for the growth of the functions of the mind. At the time of birth the mind of a child is undeveloped, and only as the child grows do its mental qualities become expressed. The gradual development of the sensory functions, bringing the child into intimate contact with his environment, makes perception possible, and perception, together with association and memory, endows the child with the capacity to form images, to think, to compare, to imagine, and to reason, and as these higher mental processes become linked up with the motor pathways, will and desire can become expressed in speech, in conduct, and in behaviour. The development of mind marches hand in hand with the development of brain, and is a consequence of the inherent tendency on the part of the brain cells to multiply and differentiate and of the stimulation of these cells by impressions from without, by the casual and haphazard incidents of experience, and particularly by those deliberate and systematic agencies which together with the imparting of definite facts and items of knowledge constitute education.

No one will deny that the capacities for mental development exhibited by different racial stocks, families, individuals, differ markedly, and the question straightway arises as to whether this difference is the reflection of deeper dissimilarity in inborn capacity for development, or whether it is due to inequality in education. Complete and long-continued isolation due to physical abnormality or to ill-treatment will result in a mental state equivalent to pathological mental deficiency. It will be granted also that if the brain is, or becomes, a faulty mechanism, through disease or defective hygiene, mental development must become embarrassed. But even among well-cared-for children coming from very similar environments and subjected to a uniform and sound training, the capacity for response and the results achieved differ markedly. Some will do well, making rapid progress under the influence of one kind of educational stimulus with very little actual instruction, whereas others will fail completely to respond, even though supplied with every facility and encouragement. Biographies show plentiful instances of men who have acquired considerable intellectual ability with but meagre orthodox educational advantages and under well-nigh impossible conditions. There can be no doubt that nurture and education play important rôles in the expression of ability since they can encourage or embarrass it, but it can be stated dogmatically that they certainly do not play the essential part. The chief factor which determines the extent and nature of the child's mental development is its intrinsic and inborn potentiality for such development. Educability is strongly inherited and rests upon the physical basis of the brain, being dependent upon keen and accurate perception, good powers of attention, memory, visualisation, comparison, judgment, well co-ordinated motor response, and these upon the healthy physiological functioning of a well and harmoniously developed brain.

The State must give into the hands of the educationalist brains capable of responding to education and see to it

that these develop in an optimum environment whilst the educationalist must provide the appropriate stimuli towards mental development. It is not equality of opportunity in education that is wanted: what is needed is that the educationalist shall be permitted to treat his students as a doctor treats his patients, individually. The ambition of the State, of the educationalist, and of the individual should be to provide full opportunities for complete expression of the inborn capacities of all who are socially worthy.

It is undoubtedly a fact that at present the most satisfactory human material for critical study are identical twins. Galton, as early as 1883, after reviewing the histories of some 35 pairs of probably identical twins, came to the conclusion that, save disease, none of the environmental conditions which had differentiated the members of the pairs had exerted any pronounced effect upon their psychological characters. This conclusion cannot be accepted finally until it has been re-examined by modern methods of psychological analysis, and until many cases of identical twins reared apart under distinctly different conditions of nurture have been thoroughly examined. Such a test to-day will examine the reliability of the tests commonly used as well as define the genetic significance of the facts which these methods reveal. There can be no doubt that the objectiveness and the absence of the personal equation in determining scores make the modern methods of investigation far superior to the older method of collecting data through the employment of untrained, often uncritical, personal opinion. However, it has to be recognised that the reliability of these modern methods has not been finally established as yet. If knowledge concerning the inheritance of human mental qualities is to be secured, as many cases as possible of identical twins reared together and reared apart must be examined, for such a study may be expected to demonstrate in the clearest fashion those differences which are genetic on the one hand, and those that are the result of different experience on the other.

A notable beginning of such a study has been made, and there has been adduced considerable evidence which shows that intelligence tests applied to adult identical twins, reared apart from the age of two weeks, yielded scores very significantly alike, despite the fact that these twins had endured great differences in the amounts and kinds of formal schooling. Such tests as the American Army Alpha Test and the Otis Advanced Intelligence Test, would seem to yield results highly correlated with the genetic basis of intelligence when applied to individuals brought up in the same general territory and social class. The non-intelligence tests, *e.g.*, motor reaction time, association time, will temperament, emotions, and social attitudes, give results in striking contrast with those of the intelligence tests in that the twins receive markedly different scores in all of them. It is concluded that such tests are of but slight value in indicating psychological differences of genetic origin. It would appear, then, that the mental qualities which certainly appear to be highly correlated with success or failure in particular vocations are not mainly hereditary. This being so, it follows that the estimates of many of the qualities assigned by untrained observers who used no system of measurement to individuals in a family history must be without any real value in genetical study. It is of the greatest importance that the psychologist shall seek better means of defining such truly genetic differences as do constitute much human psychological variation, for, even though at the present time there is very little scientific evidence concerning inheritance in the human of the kind that is plentiful in the case of many other forms, there is abundant reason for assuming that many of the differences between men are strictly genetic in origin and that it is perfectly reasonable to contemplate selective breeding as a means towards mental superiority.

It is certainly and emphatically true that as yet we are not in a position to discuss at all seriously questions of

genetic superiority, in the case of communities bound by physical, religious, or political ties, for their mental characters are in the main the outcome of imitation and of training. If it is unjust and unwarrantable to condemn a political group as being genetically inferior, it is unpardonable to utter judgment as to the relative genetic worth of different biological races. A recognition of our present lack of knowledge concerning inheritance in the human should prevent the too eager adoption of pleasing genetic speculation by those who seek biological justification for political and social prejudices.

Mankind, reading the records of its past, writes its own history. This, therefore, exhibits bias. Anthropology, the science which seeks to show which of the racial characters are para-, mixo- and idio-variations, which are genetic, and which are non-inheritable modifications, is necessarily ignorant of many crucial matters because mankind has not been exposed to controlled and critical experimentation and because many of the pages of man's history have been lost or rendered illegible.

The simplest definition of a race is a group of individuals exhibiting a certain combination of arbitrarily chosen characters in common by reason of their ancestry. The possession of a common characterisation is usually and warrantably regarded as an indication of a common ancestry. However, a common origin is not the only cause of similarity in characterisation: this may be the result of the impress of similar environmental agencies upon dissimilar groups.

Race names, Nordic, Alpine, Mediterranean, are but convenient abstractions: no race is homogeneous, and since racial characters are heritable, there is much shuffling and recombination with each succeeding generation. Within a race, however, there are plentiful pockets of relatively homozygous types, agreeing closely in respect of a certain combination of the racial characters. Differentiation of types within a race is essential for the maintenance and

development of that race, for the social organisations are complex and require diversity in the people in order that there may be differentiation in service. It is highly desirable, no doubt, that a nation should consist solely of individuals of the highest grade of physique and intellect, but no such nation could exist unless all kinds of service were held to be equally worthy of social reward and equally provocative of self-expression. If the hewing of wood and the drawing of water must remain uninspiring, and if these menial tasks must continue to be performed by a section of the people, then it would seem to be desirable that a percentage of the population that is relatively mentally inferior should exist. Whilst there are round holes in social service, there must be round pegs, and until the shape of the holes has been changed, it surely is unreasonable to change that of the pegs.

A pure race, if such existed, would be descended from a single pair of ancestors and to it there would have been no admixture from any other line of descent. No present race of man can claim such an origin It is by no means certain that mankind is derived from a single source, but even though this were so, these first ancestors are so very remote that during the succeeding 2000 generations variation has so split up their descendants that now it is impossible to prove a common origin. The distinction between a species and a genus rests upon the length of time that has elapsed since the common ancestor. The species within a genus in general must have had a common ancestor much more recently than had the genera within a family. Diversity again will be conditioned by the frequency of variation. If in one group new characters arise frequently, then this group only a hundred generations from its origin may exhibit greater diversity than another ten times as old but stable. From the first new races could arise, whilst the second would remain unchanged. The majority of differences exhibited by individuals are,

as far as can be judged, neither helpful nor harmful: they do, however, give a pleasing variety to mankind.

The distinguishing morphological racial characters are but few in number. The most obvious is skin colour, and white, brown, yellow, red, and black races are recognised. Within a race the skin colour is variable though there is but little overlapping of the races save that due to hybridisation. The skin colour is determined by the combination in varying proportions of the white of the skin itself, the red of the blood, a yellow pigment lipochrome, and a black pigment melanin, and by the differences in the racial and individual reaction to exposure to sunlight. In the full-blooded negro the proportion of the black in the combination is as high as 70 per cent.; in albinos it is not present at all; in the European its percentage is about 10, in the Japanese about 20. In the same cases the percentage of the yellow element is about 3, 5, 20, 14 respectively. It would appear that the several types of mankind differ one from the other in respect of the proportion of black and yellow pigments in their skins. The blackest pigment is found in the people on the borders of the Indian Ocean from Australia through certain parts of India to the whole of Central Africa. In the European peoples there is comparatively little black pigment, but this is developed in certain races when exposed to sunlight. In Eastern Asia there are races which on exposure develop a considerable amount of black but which have in addition a large amount of yellow.

There would seem to be a two-factor difference between the full-blooded negro and the white in respect of skin colour. The F_1 mulatto has a skin colour intermediate between the two parental colours, and in the F_2 all grades of colour from white to full black can appear. If one avoids certain complicating observations, there is no more clear-cut instance of Mendelian segregation and recombination than this. The mode of inheritance can be illustrated by ascribing

to each of the factors concerned a number to indicate its pigment-producing power, *e.g.*, A = 6, B = 4, a = 3, b = 2. Segregation in F_2 will provide a whole range of colour types. It is seen that it is possible for an apparent white to emerge from a mulatto mating and for a black child to reveal the real hereditary constitutions of apparently white parents.

Negro		White	
AABB	×	aabb	P_1
6644		3322	
20		10	
	AaBb		F_1
	15		

AABB	AABb	AaBB	AAbb	AaBb	aaBB	Aabb	aaBb	aabb	F_2
20	18	17	16	15	14	13	12	10	

It should be stated that there are records of negro × white crosses which cannot be accommodated by the above scheme. However, it will suffice for the present and will serve its purpose well if it encourages further inquiry.

In general, it would seem to be the case that when both parents are clearly blonde, all the offspring will be blonde. If one parent is blonde, and the other brunette, half the children may be expected to be blonde, the other half darker.

It is of interest to speculate as to the skin colour of ancestral man. He may have been black skinned or he may have been light skinned, or mutation could have given rise to the different skin colours of modern man. But there is no satisfactory evidence that the differentiation of mankind has been due to the direct action of sunlight. It is true that the aborigines of Central and Southern Asia are deeply pigmented, as are also the Cingalese, Papuans, and the Australian aborigines. But the Tasmanians, equally dark, lived at a latitude of 42°; the Eskimo is as dark as the equatorial Indian, and these have never attained the depth of colour of the negro. The concentration of the more

deeply pigmented races, especially in the equatorial regions, may well be ascribed to the fact that a melanic mutation occurred in a light-skinned people, and *vice versa*, and that these darker types were able to enjoy regions of the earth's surface which are inhospitable to their less pigmented competitors. The darker types which once inhabited Europe were not able to hold their own against a light-skinned people and so migrated. It is not suggested that the only difference between the two types is concerned with skin colour, but it is not impossible to think of this as the deciding factor in the survival of a type thrust out from one region into another with a different climate.

There is a patch of dark pigment over the coccyx which is present in Mongolian stocks and which, since it appears also in hybrids, is regarded as being hereditary and as an indication of Mongolian ancestry. It is to be found among the peoples of Hungary, Austria, and Moravia, and is characteristic of the Burmese babe.

Thickness of skin would seem to be a genetic character based on many factors. There are suggestions of segregation in the case of European × Hottentot crosses.

The surface of the skin is marked with lines. The flexor-creases on the palmar surface of the hand and fingers are present in the embryo. Individual differences are conditioned by the position of the muscles, the sites of articulations, the presence of small cushions of subcutaneous fat, and so forth. Since the agencies which condition the expression of these lines and creases are themselves hereditary, the lines themselves are also hereditary. The finger-print pattern is an individual character but is definitely genetic though of multi-factor origin. Identical twins often present mirror-image arrangement of the finger-print pattern, and in all cases the similarity in pattern in identical twins is greater than that exhibited by ordinary brothers and sisters. In fact, this is one of the most reliable tests for identical twins. The pattern does not change after its

assumption in embryonic life, and since the different races have different patterns, though these may overlap, it can be regarded as a racial character. For example, in respect of finger-print pattern, the Japanese, Chinese, and Koreans exhibit a general similarity, distinguishing them from all other peoples, including even the Aino.

As regards the colour of the hair, some races have dark, brown-black, or black, others have light-brown or blonde, and this latter type would appear to have originated in Europe. The study of the inheritance is complicated by the fact that the colour becomes darker during the period birth-maturity. It would seem that dark-haired children never come from flaxen-haired parents: it is a good general rule that the colour of the child's hair is not darker than that of the darker parent. An interesting observation concerning the inheritance of hair colour is that there is no intermediate colour, no blending in the hybrid. It would seem that there are two series of colours: (1) golden-blonde, golden-brown, brown, brown-black, which always include red pigment, and (2) silver-grey, ash-grey, dark-grey, black, which do not include red. The two series are based on different sets of hereditary factors which act only in the presence of a common factor determining the production of pigment. An albino is one lacking this common factor. Red is dominant to not-red, and it is observed that it is extremely rare for two red-haired individuals to marry.

Different races have hair of different shapes in cross-section; straight hair is circular, kinky hair is elliptical, wavy and curly hairs are intermediate. It is assumed that the original type was straight, and that from this the other forms have been derived by mutation. There is a postulated dominant factor which produces curling and another which produces spiral-torsion and probably still another which makes the hair stiff. In certain cases of negro × white crosses both wavy and kinky hair appear, the hair being wavy on the vertex and kinky on the sides of the head. There

are several tribes of Australian aborigines who believe that they are descended from two distinct groups which, though they intermarry, are still distinguishable by the possession of straight and wavy hair respectively. But it has been noted that the two kinds of hair are to be found on the head of one and the same person and the segregation is not so distinct as was thought.

It has been suggested that climatic conditions probably account indirectly for the character of the hair. It is difficult to reconcile this hypothesis with the observed facts that the Mongoloids have straight hair whether they are tropical Carib Indians or Arctic Eskimos, and that the negro of Central Africa has woolly hair whilst the Carib living under very similar conditions is straight haired. There is as yet no clear-cut evidence which shows how differences in hair-form become associated with differences in skin colour.

The mode of inheritance of eye-colour is one of the most clear-cut of Mendelian inheritance in the human. There are two layers of pigment, one anterior and the other posterior to the iris. In the absence of the anterior melanin layer, the iris appears yellow-brown, grey, green, or blue, the exact shade depending largely on the completeness of the absence of pigment. This absence may be a racial or an individual character, and is a recessive. Purely blue-eyed parents have none but blue-eyed children. The heterozygous blue-eyed person is one who has light brown or grey or green eyes. Dark-brown eye × dark-brown eye gives only dark-brown if they themselves are homozygous: if one or both is heterozygous, then some of the children may be green, grey, or light-brown-eyed. There are records which seem to suggest that, in addition to these autosomal factors for brown and blue, there is a dominant sex-linked factor for brown. However, it is unprofitable at this step to complicate the story which in the great majority of cases is adequate. It is highly desirable that the various grades of colour should be better defined and that their histological

basis should be demonstrated. When this is done, to trace their inheritance will be a simple task.

In the case of eye-colour, as in that of hair-form, environmental agencies do not affect the character so that these can be regarded as good racial characters. The mode of inheritance of eye-colour in racial crosses is similar to that which obtains in matings of individuals within one and the same race.

The results obtained from race crossings suggest that differences in nose-shape are based upon at least four hereditary factors inherited independently. These would seem to influence the characters of the dorsum of the nose, the shape of the alæ nasi, the root of the nose, and the tip respectively. The convex nose is dominant to the flat low one. A remarkable thickening of the underlip (the Habsburg lip) which is dominant, a shortness of the upper lip, a narrowness of the mouth, are certainly heritable characters.

The almond-shaped palpebral fissure is certainly hereditary. It is seen in the peoples of Western Asia. It is a recessive character and is often combined with strabismus. The slanting Mongolian eye with its "Mongolian fold" is encountered occasionally among Europeans and would seem to be a dominant character though its mode of inheritance is not perfectly clear.

Differences in the shape and length of the ear are controlled by many different independent hereditary factors. Free and attached lobe would seem to constitute a simple pair of Mendelian characters.

The cephalic index is regarded by anthropologists as a trustworthy criterion of race. It is of interest, therefore, to learn that the shape of the skull is a heritable character. Differences between the round head and the long head types are exhibited by the fœtus of 8 to 9 months. In spite of the fact that the skull in early life is plastic, its shape becoming modified through birth injuries or through the use of different pillows and such like, in spite of the fact that for reasons unknown a change in environment

leads to a modification in the length-breadth index, so that Jewish children in America come to possess narrower skulls than their parents whilst the skulls of Sicilian immigrants become broader, and in spite of the facts that social and language differences are responsible for differences in the facial portion of the skull, and that the length-breadth index of the skull is influenced by the length of the body, the longer the body the lower the index, so that the cephalic index is indirectly modified through general nutrition, yet all these modifying influences fail to disguise the fundamental genetic impulse towards the development of a racially typical skull form.

In a general way, brachycephaly is dominant to mesocephaly and this is dominant to dolichocephaly, and there would seem to be three factors concerned since there are three graded forms. The shape of the skull is determined by hereditary factors and modification by environment or exercise is only in a plus or minus direction. The indices of identical twins are indeed very similar. Differences in the skull form of different social groups within one race are probably due to differences in nutrition and in exercise. The characters concerned in the cephalic index do not differ in their hereditary behaviour from size and shape differences generally and have no special significance through being racial characters. There is reason for holding that skull characters are profoundly affected by the physiological action of the endocrine glands and that these may be the mechanism by which the genetic factors determine skeletal form among other racial individual characters. But this does not affect the fundamental genetic nature of these characters.

There are relatively tall races and relatively short. Apart from the variations which can readily be ascribed to environment, there are differences which are clearly inherited. Different conditions of life cannot account for all the observed differences in stature and physique. Differences in different regions of one and the same

country are usually indications of the invasion of different true-breeding types. If in an industrial area records show that the average height of the people is diminishing, then rather than quote this as an instance of the effect of a certain kind of existence upon those exposed to it, it will be well to inquire whether these conditions are not attracting those elements in a mixed population that are genetically short-statured and repelling those that are tall. The Scot is taller than the Englishman, that is, the average height of Scotsmen is greater than that of Englishmen, not because the Scot eats porridge, wears the kilt, or endures a peculiarly unattractive kind of climate, but because for genetic reasons he is potentially taller and because porridge, kilt, and climate do not prevent the expression of his hereditary constitution.

The total stature of an individual is the sum of the length of several quasi-independent parts. The Eskimo, Mongoloid, and some Amerinds have a relatively long trunk and relatively short legs, whereas the Australian aborigines and some negro groups have a short trunk and long legs. Observations seem to show that the lengths of the supra- and sub-sternal regions are independently inherited as are also the lengths of the different regions of the lower limb

Size and growth are so dependent upon the functioning of the glands of internal secretion and upon nutritional agencies generally that their genetical study is made exceedingly difficult. Occupational exercises evoke considerable modifications during development and the end-result may give an entirely false picture of the hereditary constitution of the individual. It seems probable, however, that there are hereditary factors affecting the size of the body as a whole, and others which influence the size of local parts. Stature is not a unitary thing, it is the resultant of many diverse inherited elements becoming expressed under a particular set of conditioning environmental agencies.

If both parents are tall, then all their offspring tend to

be tall: if both parents are short, some children will be tall, others short. If the four grandparents were very unlike, the grandchildren will be very variable, whereas if the four grandparents were similar in respect of height, then the grandchildren will tend to be like unto them and uniform.

Constitutional corpulence and constitutional thinness are distinctly racial characters. The Chinese, Turk, Magyar, and Jew exhibit a tendency towards corpulence: the Anglo-Saxon, Scandinavian, and Spaniard all tend towards thinness. Corpulence would appear to be the dominant of the pair. Steatopygy, the condition in which there is a large accumulation of fat on the buttocks, as seen in Hottentot and Bushman women, is certainly an hereditary character. The hybrid European × Hottentot exhibits this character only to a relatively slight degree.

It would seem that the different types of physique are in some ways related to differences in mental and temperamental attributes. But these types are not racial: all races include these types and the racial type is decided by the proportions of the varied types within it, it is a standard, an average, and often a caricature.

In a general way, if both parents are heavily built and of a heavily built ancestry, all the children will tend to be heavily built; if they are slightly built, the children will tend to be likewise. When one parent is heavily built, the other slight, some children will be heavy, some slight.

An interesting genetic difference in toe-length has been recorded. There are three forms of foot, one in which the first toe is longer than the rest (type L), one in which the second toe is longer than all the others (type S), and another in which the first and second toes are of equal length. Type L is the commonest in the adult population of England; type S is commonest in the fœtus. L is irregularly dominant to S and, while the male heterozygotes tend to be L, the females approach the S type.

There are many racial variations in musculature, shape,

and size of the internal organs recorded. The palmaris longus, for example, is different in the white, negro, Indian, and Japanese, and there are weight differences in respect of spleen and other organs between white and negro. In the matter of the brain, there are racial differences in weight. The average weight of Europeans, Japanese, and Chinese is greater than that of negroes and Australian aborigines. Differences in convolution pattern are not racial characters. There are many instances of familial peculiarities in the distribution of blood-vessels and nerves.

The fact that there are inherited differences in the size of organs and parts is of profound significance when it is remembered that it involves the inevitable sequel that racial and other crossings can lead to serious disharmony. That orthodontia is now a well-developed and important branch of dentistry is an indication that such disharmony exists, and there is every reason to hold that this is the result of the mating of different true-breeding types. Disharmony between teeth and jaws, between size of body and size of some important organ or organs, disharmony among the various components of the endocrine chain, this can result from ill-advised interracial mating. Such a disharmony is commonly displayed in difficult labour caused by disproportion in the sizes of the passenger and of the maternal passages. The Nordics have the broadest pelves, the Negroid races the smallest, and though in the same race the sizes of the fœtal head and of the pelvic outlet are in harmony one with the other, in racial crosses this harmony is disturbed.

Left-handedness is certainly inherited in some families as a simple recessive. It is more common in the male and characterises about 4 to 5 per cent. of an adult population—white as well as coloured—and occurs in the same proportion among the congenitally blind. It is of interest to note that one of identical twins is commonly left-handed. Since 10 per cent. of children are left-handed and only 5 per cent. of adults, manifestly training can convert the genetically

left-handed into right-handed. In this connection, it is of importance to remember that too strenuous attempts at such conversion are likely to be attended by the development of stuttering, following upon the involvement of the speech centre.

The manner of clasping hands, right thumb above left or *vice versa*, is heritable. It has no relation to left- and right-handedness. When both parents exhibit a left- or right-hand clasp, then the majority of their children will exhibit the same habit.

Of the physiological characters, the time of attainment of puberty, longevity, the pitch of the voice, twinning, and blood-group differences have been most studied.

There is no doubt that differences in the time during growth of the onset of puberty are familial and racial characters. Climatic and nutritional agencies profoundly affect the sexual life of man in all its phases, but when all allowances have been made for this fact, there still remain inborn differences which lead to differential rates of growth and of differentiation. The results of experimental breeding work corroborate this conclusion.

Centenarians are commonly asked for a recipe for long life. They rarely prescribe aright, for the true prescription is that he who wishes to live long should choose long-lived ancestors. The grandson of long-lived grandparents is by far the better "risk" for an insurance company than is one of short-lived ancestry.

Natural death is not a necessary or inherent attribute of life. The cell is potentially immortal and would be immortal if appropriate conditions were provided. The germ-cell is immortal and various somatic cells and tissues have been shown to be potentially immortal in tissue culture. Tissues and individuals die because of the differentiation and specialisation of structure and function which they exhibit, for such specialisation involves the loss of functional independence. The component parts of the body are so interlocked, so interdependent that a breakdown in one

wrecks the whole. It can be shown that different organ systems wear out at different rates, for the reason that all the parts of the organism are not equally perfect; the rate of evolution of the components which in their combination is man, has been unequal. The probability of any particular organ system breaking down and causing death is mathematically definite at each age and changes in an orderly manner as age advances. Thus from 1 to 60 it is breakdown of the respiratory system that is mainly responsible for death, from 60 to 90 it is breakdown of the circulatory system that is responsible. Over 50 per cent. of deaths result from a failure on the part of the organs of endodermal origin, about 10 per cent. from breakdown of organs of ectodermal origin, and the remaining deaths result from a failure on the part of mesodermal organs. Endoderm is the laggard in the evolution of man, and therefore organs of endodermal origin are least fitted for the tasks which modern civilisation sets them. Without the endoderm there would be no great need for State medicine.

The duration of life is influenced by hereditary and by environmental factors, and the task is that of discriminating between the two. There is no doubt whatsoever that there is a definite and close connection between the average longevity of parents and that of children. Extremely long-lived individuals have a much higher percentage of extremely long-lived parents than do shorter-lived children. There is no doubt that the principal determinant of longevity is heredity, and the average duration of life of a population cannot be modified at all profoundly by any sort of improvement in State medicine. The age at which an individual dies is determined by the biological constitution of the individual, and it is estimated that 50 to 75 per cent. of all deaths are determined by hereditary factors leading in their action to this or that kind of breakdown. The death-rate during the earlier age periods of life is selective, eliminating the biologically unworthy and leaving the biologically strong. Child welfare salvages the weakly who may

grow up and reproduce: but they will breed true to their constitution. More often, however, the application of medical skill merely postpones death for a little while; the infant that would have died in its first year is kept alive to die in its third.

It is not without significance that the mortality among children of the age group 1 to 5 varies with the age at death of the parent. The longer lived the parent is, the lower the mortality among the children. Thus if the parents were such as live till 80 and more, the death-rate of the children of 1 to 5 years is but one-third to one-half of that of the 1 to 5 age group as a whole.

An individual is a machine so constructed genetically that it can perform, before it dies, a certain limited amount of work, mechanical, chemical, and other. The total energy output is predetermined by the genetic constitution of the individual. The rate per cent. of time of energy expenditure is influenced within wide limits by environmental agencies and therefore these, by influencing the rate, influence the duration of life itself. Occupational hazards will, of course, overwhelm any genetic bias towards long life as will also any extravagance in living, but essentially duration of life is a genetic character, and in the case of relatively pure races is a distinguishing racial character.

It is now well known that there are in the serum of blood definite substances that agglutinate the cells of blood from other persons. These specific substances which cause the clumping of the cells are known as agglutinins. The equally specific receptors in the red-blood corpuscles are called agglutinogens. According to the mutual behaviour of their bloods, individuals can be classified into four groups:

Group.	Effect of Serum.	Capacity of Cells.
I	agglutinate cells of II, III, IV	Not agglutinated by any serum
II	" " III, IV	Agglutinated by serum of I, III
III	" " II, IV	" " I, II
IV	does not agglutinate any cells.	" " I, II, III

Agglutinin A is the one present in group II. Agglutinin B is that found in group III. Group IV has both A and B, group I neither. This is not the system of classification commonly used in Britain.

Within each race there occur definite and characteristic proportions of the four groups. These characters, based upon the presence and action of two dominant mutant genes, and capable of being studied biochemically, afford a means of investigating racial origins and relationships. For example, European populations show a preponderance of the agglutinogen A and a low percentage of agglutinogen B. Another group, Mongolian and Ethiopian, show a low percentage of A and a high percentage of B. The third group, Russians, Turks, Arabs, and Jews, contain approximately equal proportions of A and B. Most authorities are content to regard the interpretation of the observed facts on the assumption that two-factor pairs are involved as adequate, but others hold that these facts require the operation of a series of three multiple allelomorphs. The two-factor pair interpretation is as follows. Factors A and B (corresponding to the agglutinins A and B respectively) are dominant, a and b (their respective iso-agglutinins) are recessive. In any given individual one of the following factorial combinations may be present :—

AABB, AABb, AaBB, AaBb,	corresponding to	IV
AAbb, Aabb	„	„ II
aaBB, aaBb	„	„ III
aabb	„	„ I

It is suggested that the agglutinogens A and B respectively are each characteristic of a distinct ancestral human type, a North European stock AAbb and a Central Asian stock aaBB, and that the occurrence of the other blood groups is a consequence of their intermingling. It has been pointed out that a point of considerable interest emerges from this suggestion. It is seen that of the four groups, that which has both A and B should be more common than those which have either A or B. The double recessive aabb, being homozygous, will breed true and will increase in any mixed population. Now, in point of fact, in all the records of blood grouping which now exist,

group IV (A + B) is never so proportionally strong as are groups II and/or III. This being so, it would seem that some cause exists which embarrasses the production of the A + B group. It may be that the types AABB, AABb, and AaBB cannot exist, the action of three dominant factors being lethal, so that only the AaBb type remains in group IV, or it may be that a double-dominant-bearing gamete (AB) cannot exist or, if it exists, cannot function, the AABB form being infecund and only a proportion of the gametes of the forms AABb, AaBB, and AaBb being functional.

It is quite simple to foretell what the blood group of the offspring of the mating of any two of these individuals will be. It is equally simple to diagnose the blood groups of the parents from an examination of the reactions of their offspring. The test is one that is available in medico-legal cases, for by its use it is certainly possible in certain cases to state that a particular individual could not have been the parent of a certain child.

Mating.	Blood Groups of Offspring.	Mating.	Blood Groups of Offspring.
Group I × I. .	I	Group II × III. .	I, II, III, IV
„ I × II. .	I, II	„ II × IV. .	I, II, III, IV
„ I × III. .	I, III	„ III × III. .	I, III
„ I × IV. .	I, II, III, IV	„ III × IV. .	I, II, III, IV
„ II × II . .	I, II	„ IV × IV . .	I, II, III, IV

It is claimed that the Manoilov test[1] can be employed successfully for the identification of race. Jew has been

[1] The Manoilov test consists in taking blood from the cubital vein, making a 3 to 5 per cent. emulsion of red-blood corpuscles in saline and adding the following reagents drop by drop.

1. A 1 per cent. solution of	methyl-blue (Grübler) . . .	1 drop
2. A 1 „	krezil violet (Grübler) . . .	5 drops
3. A 1·5 „	silver nitrate	3 „
4. A 40 „	hydrochloric acid . . .	1 drop
5. A 1 „	potassium hypermanganate . .	3-5 drops

After the addition of each reagent the test-tube is shaken. The shade of the colour of the end-result indicates the difference between the races (and also between the sexes). Jewish blood gives a paler colour than does Russian.

distinguished from Russian thereby and in mixed marriages the influence of the two races upon the offspring can be detected.

Twinning is most certainly a familial character. There are records of related women who have never had a single child at a birth in a sequence of pregnancies. Twinning occurs more often in large than in small families. It is found that twins occur with nearly equal frequency in the pedigrees of fathers and of mothers respectively, of families in which twinning has occurred more than once. This observation is of importance in that it suggests that this tendency to twinning is not transmitted solely through the female but through the male as well. In a family in which there are two or more pairs of twins it can be assumed that the hereditary influence of the father concerning twinning is approximately equal to that of the mother.

Identical twins (monozygotic) have their origin in the complete bipartition of a single fertilised ovum or in the formation of two buds from one ovum. They are genetically identical and are always of the same sex and are remarkably alike. For example, in the matter of finger-print pattern there is a great tendency for the formation of mirror images, especially on the forefinger. Fraternal twins (dizygotic) arise in two distinct ova, each fertilised by a different sperm. They may or may not be of the same sex and are no more alike than ordinary brothers and sisters born at different times. It is estimated that about 25 per cent. of twin births are identical twins. About 1 in 80 births is a twin birth and about 1 in 300 is identical. The production of identical twins, therefore, is dependent upon an hereditary tendency on the part of the ovum to develop into two embryos instead of into one, and upon the ability of the two individuals thus arising to complete their development. Such a tendency is reminiscent of the polyembryony that is normal in such a form as the Armadillo. The production of fraternal twins is dependent upon the extrusion of two ova from the ovary

more or less synchronously, their fertilisation and their power of completing their development. It is not without interest to note that in the case of a woman who had had several twin births there were two ova within each Graafian follicle. There are reasons for thinking that as many as 5 to 6 per cent. of all ovulations are double; they are far more common than are twin births. That this is so is due probably to the non-fertilisation of one of the ova or to early death of one zygote.

There are indications that a tendency to produce fraternal twins[1] behaves as a recessive character: but the genetic nature of this tendency is not yet clearly understood. It is of interest to note that only in 5 to 6 per cent. of cases does a woman have more than one pair of twins, the rest being singles. It is possible that twinning is rare in cases in which more than one ovum is available for fertilisation at one and the same time for the reason that one consequence of the fertilisation of one ovum is that fertilisation of others is rendered difficult or impossible and that twinning in these cases occurs because for genetic reasons this barrier to multiple fertilisation is weak. Such circumstances would at least permit an understanding of how it may be that the tendency to twinning is inherited through the male parent. From what is known of the effect of nutrition upon multiple births in domesticated animals, it can be expected that in a twin-producing strain of humans the production of twins will be conditioned by the quality and quantity of food.

There are indications that the types of singing voice are hereditary, the male bass and the feminine soprano being dominant to male tenor and female contralto, while baritone and mezzo-soprano are the heterozygous forms. The Nordics are richer in basses, the Mediterraneans in tenors.

Differences in temperament and disposition between different peoples are largely due, no doubt, to differences in social inheritance. The contact between character and

[1] See pedigree in Appendix.

environment is so intimate that it must be, by the very nature of things, most difficult to define psychic characters in biological terms. So far the distinctions between mind and mind have been crude and popular for the reason that accurate psychological analysis of the constitution of the mind as a basis for the study of inheritance of mental characters has been imperfect. However, at the present stage of our knowledge, it is possible to speak with confidence of racial mental difference and to refer to a race type which, though modified through its education, is fundamentally unaltered.

The Nordic race, tall, blue-eyed, and dolichocephalic, as compared with the short, stocky, brown-eyed brachycephalic Alpine, is the builder of empires, the creator of cultures. Prudent, reserved, self-controlled, its sensuous instincts are subordinated to higher aims. Courageous, seafaring, athletic, mentally active, with capacity for organisation based upon sound judgment; ambitious, enterprising, individualistic, given more to natural science than to history and philosophy, thinking in pictures, finding beauty mainly in form, inclined towards metaphysics and to a tragical conception of life, these are the characters of the Nordic.

Along the Atlantic seaboard the people exhibit a deep love of home and of convention. They are inclined towards meditation and mysticism, are self-willed, obstinate, reserved.

The Mediterranean peoples, small, slender, brown-eyed, dolichocephalic, are vivid, volatile, appreciative of shape, line, colour, gesture, and of the spectacular. Passionately given to the occupation of the moment: easy in self-expression, and given to extravagance. Take life not too seriously, and are not renowned for adherence to truth or to loyalty.

The Oriental is marked with energy and enterprise. Nomadic, inventive, creator of culture.

The Jew, Greek, and Armenian are clever and intuitive; have no capacity to form a political state but flourish as minorities among other peoples. Inclined to abstrac-

tion, logic, and dialectic, highly musical, eloquent, monotheistic.

The Mongolian is highly social, more potent in reproduction than in invention, memory greater than critical intelligence, peaceable, resistant to pain, inclined to cruelty, not passionate, inactive, tenacious. The Japanese include many non-Mongolian elements and are therefore more martial and cling less to convention. The mongoloid elements among the Russians are mentally slow, superstitious, conventional, unenterprising, enduring pain calmly.

The Negro lives dangerously, is improvident, boisterous, or else dejected, lacking creative power, imagination, and ambition, is cruel, oratorical, and has no ability for organisation.

It has been shown that there is a significantly close resemblance between individuals with regard to mental as well as to physical traits and that this resemblance can be measured with a very fair degree of accuracy by the method of correlation. The co-efficient of correlation between children in the same family is about the same for mental as for physical characters. This observation cannot be reconciled to the view that environment is paramount in determining mental abilities.

It is impossible, of course, to use races as experimental material with which to demonstrate the genetic nature of the racial characters. However, it is possible to follow the mode of inheritance of these characters when exhibited by individuals. There can be no doubt, for example, that outstanding musical ability, talent in painting, and in sculpture, mathematical and technical ability, political prowess, are family affairs. Moreover, since it is the custom for members of one talented family to marry members of another talented family, the workings of the hereditary mechanism become clearly revealed. In point of fact, the occurrence of an exceedingly talented individual in a family in whose ancestry there is nothing but mediocrity is sufficient to

arouse the suspicion that illegitimacy is responsible, since mutation is rare, but it has to be remembered that pedigrees are imperfectly known and that it is not impossible for the chance recombination of the factorial ingredients of exceptional ability to account for the sudden appearance of a brilliant individual in an unexceptional family.

Exceptional ability and genius are probably due to a chance and fortunate concatenation of circumstances, the congregation of complementary genes and a peculiar environment. If this is so, it is not likely that genius will beget equal genius, but it is to be recognised that genius has a much better chance of doing so than the individual of average ability. This is the genetical criticism of hereditary titles conferred in the first instance as a recognition of exceptional ability. It is not certain that such ability will be transmitted, for the offspring has a biparental origin, and it cannot be assumed that the eminent parent was duplex for all the factors which underlay his ability. A title can outlive any expression of ability in its possessors, and when once the genetic basis of this ability is lost, it can only be regained by out-crossing. There may be biological endorsement for the marriage of the European nobleman and the colonial heiress. Whether there is or not will depend upon the quality of their offspring and these are somewhat rare.

Though genius is difficult to define, and to assess, it can be recognised. It is a matter of greater difficulty to demonstrate conclusively that average degrees of ability are likewise heritable. At present no really satisfactory intelligence test is available. But using such as are available, there is no difficulty in showing that ability of this grade is a family affair, that relatively clever children have had relatively clever parents who invariably belong to the higher social grades and trades and professions. A rigid caste system runs right through the most democratic of states.

Similarly, education does not lead to equal advance, it merely emphasises the initial difference: the relatively bright child, being bright, profits more from educational stimuli. When the school records of parents are dissimilar, then those of the children are more dissimilar than those of children whose parents had more or less similar records. Education does not evoke similarity in grade of ability as is seen in the case of orphans reared in the same atmosphere. Fraternal twins, reared together, are usually markedly dissimilar in their attainments. Identical twins, reared apart, are markedly alike in character, temperament, and talent.

There are indications that irritability is a temperamental character behaving as a simple dominant to calm, as is joyous to sad; that nomadism is inherited, but manifestly the accurate analysis of such qualities is exceedingly difficult. Peculiarities of gait, gesture, general bearing, blushing, are inherited, and the mode of their inheritance follows the established laws. They are not always instances of imitation. For each of these there is a physical basis, and a consideration of the minuteness and variety of differences that are inherited will enable the student to attain a truer perspective regarding the whole field of heredity and variation. The evidences of organic inheritance are universal.

When all allowances have been made for the modifications of a characterisation by the impresses of a varying environment, there still remain characters essentially unchanged, being inborn. It is impossible to agree with the dictum "change the nations in their cradles, and Semites will grow out of Aryans and out of Aryans, Semites" unless the characters that distinguish the two are such as pertain to the social and not to the organic inheritance. Two text-books of embryology, dealing with the subject minutely and in detail, but based on studies of different biological races, will not agree on many a point, for distinguishing the races there are different developmental impulses which lead to different kinds, degrees, and rates of development and differentiation.

Two hundred generations or so ago the ancestors of the modern civilised peoples were, it may be safely assumed, very much as the Australian black man is to-day, gatherers, capturers, appreciating comfort yet not creating it, enjoying the warmth and protection of clothing yet not making it, reaping the harvests of the earth but never sowing, spending long days of arduous labour and yet not taking steps to make existence easier. The question thus arises as to whether our ancestral stocks were genetically equivalent to the present day aborigines of Australia, who are what they are either for lack of opportunities or in virtue of their genetic mental equipment. It is the opinion of most authorities that it is not possible by any system of education to convert an aboriginal tribe into a civilised community. The modern civilised peoples come of an ancestry that has been passed repeatedly through the fine meshes of the sieve of civilisation, those individuals and those stocks whose mental abilities fitted them for the discipline of civilisation passed through: those which have refused to accommodate themselves to the demands of changing social orders have been rejected and eliminated. The destiny of a race is determined by its genetic composition. The Australian black man is doomed since he must be overwhelmed by a social order which cannot accommodate him.

CHAPTER VII

INHERITANCE IN MAN

2. *Abnormality*

IF the abnormal character is an autosomal dominant to normality, it will be exhibited by individuals either duplex (AA) or simplex (Aa) for the factor concerned, unless the expression of the character is conditioned by environmental agencies. The following matings are possible :—

Affected (duplex)	×	Affected (duplex)	giving	all affected (duplex)	AA
,, ,,	×	,, (simplex)	,,	50% ,, ,,	AA
				50% ,, (simplex)	Aa
,, ,,	×	Normal (nulliplex)	,,	all ,, ,,	Aa
,, (simplex)	×	Affected (simplex)	,,	25% ,, (duplex)	AA
				50% ,, (simplex)	Aa
				25% normal (nulliplex)	aa
,, ,,	×	Normal (nulliplex)	,,	50% affected (simplex)	Aa
				50% normal (nulliplex)	aa
Normal (nulliplex)	×	Normal (nulliplex)	,,	all normal (nulliplex)	aa

If the abnormal character is an autosomal recessive to normality, it will be exhibited only by such as are duplex (aa) for the factor concerned. The individual simplex for this factor (Aa) will be a carrier of the factor, but will not exhibit the character. The following matings are possible :—

Affected (duplex)	×	Affected (duplex)	giving	all affected (duplex)	aa
,,	×	Carrier (simplex)	,,	50% ,,	aa
				50% carriers (simplex)	Aa
,,	×	Normal (nulliplex)	,,	all carriers (simplex)	Aa
Carrier (simplex)	×	Carrier (simplex)	,,	25% normal (nulliplex)	AA
				50% carriers (simplex)	Aa
				25% affected (duplex)	aa
,,	×	Normal (nulliplex)	,,	50% carriers (simplex)	Aa
				50% normal (nulliplex)	AA
Normal (nulliplex)	×	Normal (nulliplex)	,,	all normal (nulliplex)	AA

If the abnormal character is sex-linked, the following matings are possible. It is to be noted that since the factor

for a sex-linked character is resident upon the X-chromosome and since the male has but one X, the male is constitutionally simplex for the factors for sex-linked characters, and cannot, therefore, be a carrier in whom this factor is balanced by normality.

Affected male	×	affected female	giving	all affected offspring
„	„	× carrier	„	normal sons, affected sons, carrier daughters, and affected daughters
„	„	× normal	„	normal sons and carrier daughters
Normal	„	× affected	„	affected sons and carrier daughters
„	„	× carrier	„	normal sons, affected sons, normal daughters, and carrier daughters

It will be useful to give in tabulated form a list, even though incomplete, of defects and derangements which have been recorded as being inherited. In many cases the mode of inheritance is clear-cut; in others there is still uncertainty as is to be expected, for the records are culled from family histories and have not been secured from critical experimentation.

In this list by *intermediate* is meant that dominance is incomplete and that the hybrid exhibits a characterisation which appears to be a blend of the parental characters concerned. By *irregular* is meant that the degree of the expression of the character is variable so that in certain cases the character is a cryptomere (hidden though present). In certain instances different pedigrees indicate that the mode of inheritance of the character is sometimes that of a dominant, whilst in others it is as that of a recessive. * = a pedigree given in the Appendix. Repetitions in the list are meant to make reference simpler.

Achondroplasia	Dominant?
Acoustic tumours	Dominant
Adenoid disposition	Dominant
Adiposity	Dominant
Albinism*	Recessive
„ limited to the eye*	Recessive (sex-linked)
„ partial (spotting)	Dominant
Alkaptonuria	Recessive
Alopecia	Dominant

Amaurotic family idiocy	Recessive (Jews: sub-lethal)
Anencephaly	Recessive
Angioneurotic œdema*	Dominant
Anidrosis	Recessive (sex-linked)
Aniridia*	Dominant
Anodontia	Recessive (sex-linked)
Anonychia	Dominant
Anophthalmia	Recessive
Arteriosclerosis	Dominant
Asthenia	Dominant
Asthma	Dominant (Recessive: sex-linked)
Astigmatism	Dominant
Ateliosis	Recessive
Atheroma	Dominant
Atrophy of auditory nerve	Dominant
Baldness (early)	Dominant (sex-controlled: males)
Brachydactyly*	Dominant
„ Hypo- and brachyphalangy	Dominant (brachyphalangy: sub-lethal)
Bimanual synergia	Dominant (irregular)
Bullosis connata*	Recessive
Camptodactyly	Dominant
Carcinoma*	Dominant? (Recessive in the mouse)
Carpal displacement	Dominant (sex-linked?)
Cataract	Dominant
Catlin Mark	Dominant (irregular)
Cerebellar ataxia	Dominant
Chondrodystrophy, non-severe	Dominant
„ severe*	Recessive
Chorea*	Dominant
Cleft-palate	Dominant (irregular)
Clinodactyly	Dominant
Clubbed fingers	Dominant
Club-foot (Pes varus)*	Recessive
Coloboma iridis	Dominant (irregular: mostly males)
Compulsive insanity	Dominant
Congenital absence of calvaria	Recessive
Congenital hypertrophy and dilatation of lower part of colon.* (Hirschsprung's disease)	Dominant
Corneal opacity	Dominant
Corpulence	Dominant
Cretinism*	Recessive
Cryptophthalmus	Recessive

Cyclopia	Recessive
Cystinuria	Dominant
Deaf-mutism*	Recessive
Dementia amauroticans: appearing in infancy*	Recessive (almost exclusively in Jews: sub-lethal)
Dementia amauroticans: appearing in childhood	Recessive (in non-Jewish children)
Dementia præcox*	Recessive (multifactor)
Dermatosis Darier (Psorospermosis vegetans)	Dominant
Diabetes mellitus	Recessive (irregular)
„ insipidus	Dominant
Diathesis: adenoid	Dominant
„ dystrophic	Dominant
„ exudative	Recessive (sex-linked: in some cases, Dominant)
„ lymphatic	Dominant
Distichiasis	Recessive
Dupuytren's contraction	Dominant
Dysostosis cleido cranialis	Dominant
„ cranio-facialis	Dominant (irregular)
Ear, absence of external	Dominant (irregular)
„ bilobed or deeply pitted	Dominant (irregular)
Ectopia lentis	Dominant
„ pupillæ	Recessive(sex-linked: irregular)
Elephantiasis	Dominant
Embryotoxon	Dominant
Enuresis nocturnal	Recessive?
Epicanthus	Dominant (in most cases)
Epidermolysis bullosa: dystrophica*	Recessive
„ traumatica*	Dominant
Epilepsy*	Dominant (Recessive: sex-linked)
„ muscle clonus	Recessive(restricted to Sweden)
Epispadias	Recessive
Exostosis	Dominant
Eye-colour, Tortoiseshell	Dominant
Eyelids, constricted	Dominant
Feeble-mindedness*	Recessive (Dominant)
Flat-foot	Dominant
Flocculus iridis	Multifactor (one probably sex-linked)
Fragilitas ossium (+ Blue sclerotics)	Dominant (especially in Jews)
Freckles	Dominant
Friedreich's ataxia*	Recessive
Gallstones	Dominant
Glaucoma	Dominant(sometimesRecessive)
Glioma	Recessive?

Glomerulo-nephritis	Dominant
Glycosuria: non-severe	Dominant
„ severe	Recessive
Goitre: endemic and sporadic	Dominant
Gout	Dominant (irregular)
Gower's disease (saltatory spasm)	Recessive (sex-linked)
Hæmophilia	Recessive (sex-linked: sub-lethal)
„ pseudo-	Dominant
Hæmorrhagic telangiectasis	Dominant
Hallux valgus	Dominant
Hare-lip	Dominant (irregular)
Hay fever	Dominant
Hemeralopia*	Dominant
„ if with myopia	Recessive (sex-linked)
Hereditary epistaxis	Dominant
„ spinal ataxia*	Recessive
„ tremor	Dominant
Hermaphroditism mascularis externus	Recessive
Heterochromia iridis	Recessive (irregular)
High blood-pressure	Dominant
Hirschsprung's disease*	Dominant
Hydro-æstivale	Recessive
Hydrophthalmia	Recessive
Hyper-extension at joints	Dominant
Hyperidrosis	Dominant
Hypermetropia	Dominant
Hyperphalangia pollicis	Dominant?
Hyperthyroidism	Dominant
Hypertrichosis	Dominant
Hypoplasia	Recessive
Hypospadias	Dominant (irregular: sex-controlled males)
Hypotrichosis congenita*	Dominant(irregular)(Recessive)
Hysteria	Dominant
Ichthyosis congenita*	Recessive (sub-lethal)
„ vulgaris*	Dominant (irregular)
Infantilism	Recessive
Infundibular thorax	Dominant (irregular)
Inguinal hernia	Dominant
Insanity, maniac depressive*	Dominant
Jaundice (hereditary)	Dominant (intermediate: irregular)
Keratoconus	Recessive (or multifactor)
Keratosis universalis*	Recessive
„ follicularis	Dominant
„ follicularis spinulosa decalvans	Intermediate (sex-linked)

Keratosis palmaris et plantaris	Dominant (Recessive)
Lagophthalmus	Dominant
Leuconychia	Dominant
Luxatio coxæ congenita *	Dominant (irregular)
Megalocornea	Recessive (sex-linked)
Microbrachycephaly	Recessive
Microcephaly	Recessive
Micromelia, infantile	Recessive
„ Hanhart's	Recessive
Microphthalmia	Recessive (in some histories sex-linked)
Migraine	Dominant (sex-linked)
Monoletrichosis	Dominant (irregular)
Muscular dystrophy *	Recessive (also Dominant : sex-linked)
Myoclonus epilepsy *	Recessive (Myoclonic)
Myopia *	Recessive (Dominant: irregular)
„ hemeralopia	Recessive (sex-linked)
Myotonia atrophica	Dominant?
„ congenita (Thomson's disease)	Dominant
Neurasthenia	Dominant
Neuritis optici *	Recessive (sex-linked: irregular)
Neurofibromatosis	Dominant (irregular)
Nomadism	Recessive (sex-linked)
Nyctalopia *	Recessive
Nystagmus	Dominant
„ +swaying of head	Recessive (sex-linked)
Œdema of legs, hereditary (Milroy's disease)	Dominant
Optic atrophy	Recessive (sex-linked: irregular)
Osteopsathyrosis	Dominant
Otosclerosis	Dominant (in some histories, Recessive)
Oxycephaly	Dominant (Recessive)
Paralysis agitans	Recessive (in one pedigree, Dominant)
Paroxysmal myoplegia	Dominant (irregular)
Patella, absence of	Dominant
Pemphigus connatus *	Recessive
Pernicious anæmia	Dominant?
Peroneal atrophy	Dominant
Pityriasis versicolor	Recessive (sex-linked)
Polycystic kidney disease	Dominant
Polycythæmia	Dominant
Polydactyly *	Dominant (irregular)
Prognathism	Dominant
Progressive muscular atrophy	Recessive (sex-linked)

Pseudo-hermaphroditism	Recessive
Pterygium	Dominant
Ptosis	Dominant
Rachitis*	Dominant
Radio-ulnar olisthy	Dominant
„ synostosis	Dominant (intermediate: sex-linked)
Red-green blindness*	Recessive (sex-linked)
Relaxation of the eye-lids	Dominant
Retinitis pigmentosa	Recessive*: Dominant* sex-linked*
Rounded back	Dominant
Scarlatinal nephritis*	Recessive
Schizophrenia*	Recessive (multifactor)
Sclerosis	Dominant
Scoliosis	Dominant
Sickle-celled anæmia	Dominant (only in negroes)
Spasmodic torticollis	Recessive
Spastic paraplegia*	Dominant (Recessive: in one history sex-linked)
Spastic spinal paralysis*	Dominant (Recessive)
Splenomegaly	Dominant (irregular)
Split hand	Recessive
„ foot	Dominant
Stammering	Dominant (irregular)
Steatorrhœa congenital	Recessive
Stenosis of mitral valve	Dominant (usually sex-linked)
Strabismus	Recessive
„ + hypermetropia	Dominant
Struma sporadica idiotypica	Dominant
Suicide*	Dominant
Syndactyly	Dominant
Synphalangy	Dominant
Teeth, absence of canines	Recessive
„ absence of molars	Recessive
„ early decay of	Sex-controlled (female)
Torsion neurosis	Recessive
Trophoneurosis	Recessive
Urticaria	Dominant
Valvular disease of the heart*	Dominant
White forelock (a white patch of hair)	Dominant
Xanthomatosis	Dominant (irregular)
Xeroderma pigmentosum	Recessive (sub-lethal)
Zygodactyly	Dominant (irregular)

In the discussion of a subject so vast and so vague as this of heredity and disease, it is most necessary to define terms. In view of the great diversity of attitude among

medical men towards this subject, it is not surprising that there should be a corresponding diversity of connotation connected with the term heredity. By genetic or hereditary factors are meant those innate forces which direct development thereby leading to definitive form in the presence of adequate and appropriate environmental circumstances. The end-result of development and differentiation, the characterisation or phenotype, is the reaction between genetic factors, the genotype and the environmental or paratypic factors. Disease, defect, derangement may be considered as any marked deviation from the standard of normality, in form or in function. Any novel characterisation, when it first appears, is abnormal, but it may be an opportunity for further evolution or it may be the expression of a disharmony which damns its exhibitors. Disease is a relative conception and does not admit of strict definition since that which is abnormal in the case of one animal or tissue is normality in another. Differences in the amount of cutaneous pigment distinguish albino, Northern European, and Southern European, and the difference between the latter two is normality, that between albino and Northern European, no greater, renders the albino abnormal, yet abnormality is determined by the same processes as is normality. Disease itself is a perturbance which contains no elements essentially different from those of normality, but these elements are presented in a different and less useful order. It is the state of an individual at the limits of its accommodation.

All the abnormal characters to which reference has been made are to be regarded as the results of the interference in the normal seriation of events in development by genetic factors. The digital abnormalities, for example, are reflections of irregularity in the formation of crenations on the free margin of the embryonic hand rudiment. Such irregularity either in space or time leads to corresponding abnormalities in the differentiated hand. The genes

involved are such as effect a particular event in development. Palatal defects are the expression of the action of genes which in their action interrupt the usual fusion of the bilateral elements of the developing palate. In amaurotic family idiocy the action of the gene leads to a disharmonious rate of development of the sensory nervous system; in feeble-mindedness there results an incompleteness in the development of the cerebrum. In fragilitas ossium the gene disturbs the formation of the Haversian system of bones. There is a physical basis for all these abnormal characters, and in all cases the abnormality results from a definite disharmony in the processes of development. It would seem that the genotype is an unbolting mechanism, the genes coming into action serially and releasing physiological agencies which specifically affect development. If, for example, there are genes which determine the time at which the pituitary comes into action during development and which determine the rate of its functioning, then mutation can result in profound disturbance. Further, the mingling through marriage of two genotypes can equip an individual with, for example, a quickly developing soma and a slowly differentiating pituitary, if these are segregating characters, and the end-result can be such a condition as chondrodystrophy, certain forms of which can be interpreted as the result of a retardation in the exhibition of the internal secretion of the pituitary and a consequent unchecked, unguided ossification.

That the list of heritable abnormalities is so heavily starred with the qualification "irregular" is not surprising. There can be no doubt that in many an instance the suggested dominance or recessivity is not the true statement of the hereditary relationship of abnormality and normality. In many a case it will be discovered that, in addition to the particular gene responsible for the condition, there are several accessory genes, which in their action modify the expression of the principal one, affecting the

degree and the direction of its action. Many pedigrees show anomalies which would appear to indicate that the simplex and the duplex states of the gene respectively yield differences in the degree and direction of the expression of a character. Other anomalous pedigrees are to be explained by the fact that the expression of a particular abnormal character occurs only several years after birth and so death in infancy will lead to unusual ratios. Other anomalies are to be explained by the fact that certain abnormal characters for their expression require a peculiar set of environmental circumstances and that this has not attended the development of all the individuals concerned. Since many of these abnormal characters are fashioned by abnormalities in the functioning of the endocrine glands, it is not surprising that in many cases adjustment among the members of this system can lead to the more or less complete repair of a genetic disharmony. The individual, plastic, possessing wonderful powers of adjustment, overcomes its abnormality, but nevertheless will transmit its genes for the abnormal character which it itself does not exhibit. In the heterozygotes, the decision as to which of the two characters, normality and abnormality, shall be exhibited may be decided by the internal environment, the general physiological state of the body as a whole, and by the external environment. In one sex, with its peculiar physiology, one member of the pair of characters may become expressed, in the other sex, the alternative. So also the carrier of a sex-linked character may or may not exhibit a grade of the characterisation: this will be determined by the interaction of all her genes and by environmental circumstances.

In the case of the diatheses these may be defined as different physiological characterisations, corresponding to different genotypes conditioned in their expression by environmental agencies, which determine the individual's reaction, successful or unsuccessful, to the stresses of the

act of living. These genotypes are handicapped in the race of life. There are individuals who, in virtue of their genotypes, are predisposed to one or other of the following conditions, duodenal ulcer, peptic ulcer, chronic nephritis, pernicious anæmia, asthma, tuberculosis, gout, gall-bladder affections, high blood-pressure, urinary calculi, migraine, and so forth. These conditions, of course, can present themselves in individuals who are not hereditarily predisposed to them as a result of physiological extravagance or mishap, but the facts that there are definite asthenic, dystrophic, exudative, lymphatic, and adenoid diatheses, that it is entirely reasonable to speak of a hypersthenic gastric diathesis, of a genetic tendency for the islands of Langerhans to undergo degeneration, for hypopiesia and for many kinds of biochemical disharmonies demand a new point of view in medicine.

Legitimate fun is made of the marriage health certificate: the community is advised that Cupid is a better guide in mating than any medical board could possibly be. This may be, and possibly is, true, but until Cupid changes his primitive weapons for the highly complex armamentarium of the modern physician, it is difficult to see how he can recognise the constitutional factor in disease and practise really sound preventive medicine, which, after all, is not the monopoly of the profession but the duty of every individual.

The sound treatment of those diseases which are based in diatheses is that which concerns itself with the recognition of this constitutional factor before the diseased condition is exhibited and in the neutralising of the tendency. All relatives of individuals suffering from such constitutional diseases should be examined and treated. The correction of the tendency and not only the cure of the disease should be the endeavour of the profession.

The question of the possible relation between certain types of bodily conformation and certain diatheses and temperaments is of great importance. It is established that the endocrines are concerned in the regulation of

the effective reactions which are associated with environmental stimuli and which tend toward action appropriate to a given situation. It is established also that these glands are concerned in the regulation of somatic growth. It follows then that there must be a close association between bodily conformation on the one hand and temperament or emotional attitude on the other, and that a disturbance of endocrine activity, genetic in origin, will reveal itself both in somatic peculiarity and in an alteration of the emotional attitude of the individual. It becomes possible, therefore, to speak of the contrasted Quixote and Sancho types of combinations of bodily and mental characters. A steatic type of woman is recognised. Lymphatic of habit, exhibiting a tendency towards adiposity, with thick greasy skin and smooth unruly hair, lazy and with pronounced sexual proclivities, negativistic and dissocial in temperament, foul-mouthed, vain, given to exhibitionism, such are the favourites of the sensual Oriental and the potential recruits of European prostitution. The equivalent male type is the Kobold, so-called because of its resemblance to the mythical goblin of German folk-lore. Short, thick-set, large-boned, strong-jawed, insensitive to pain and dissocial, the Kobold type is the most intractable of the morally deficient. Such are instances of genetic characterisations based upon the action of genes which are phthersigenic, a term used by Auden to define those hereditary factors which are deleterious in their action, tending towards the elimination of the stock. Other well recognised types are the athletic, the asthenic, and the pycnish. The athletic is powerfully built with hypertrophic musculature, with thick collar-bone, large hands and feet, skin elastic, and slight deposit of fat on trunk. The asthenic is thin and underdeveloped, with narrow shoulders and poorly developed limbs, long flat narrow chest, belly flat, but little subcutaneous fat. The pycnish is short and thick-set, with slender shoulders, thick neck, with tendency to deposit fat on trunk and

belly. Each type has its own tendencies in the matter of disease.

Of the abnormal psychological characters, feeble-mindedness merits further discussion. It is defined, not by the geneticist, but by the mental specialist, as a state of mental defect due to incomplete or imperfect development. A feeble-minded person is relatively ill-equipped mentally when compared with a certain standard of mental ability, and this standard must, of course, vary in different communities. An African Bushman may be entirely competent to look after his own well-being in those conditions to which he is accustomed, but he may be hopelessly incompetent when transplanted to a highly industrialised community. Only when it has been shown that it is absolutely impossible, in spite of all education and opportunity, for an individual ever to become able to compete successfully with his fellows can he be regarded as relatively feeble-minded.

Doubtless, in many an instance, feeble-mindedness is acquired by an individual during the period conception-death as a sequel of some accident or disease which induces arrest or even decadence of mental development. However, there are abundant reasons for holding that all feeble-minded persons are not the victims of such accidents during development but that many of them were feeble-minded *ab initio*, that the condition which they exhibit was truly inborn, for records of countless family histories from all grades of society suggest in the strongest possible manner that feeble-mindedness is transmitted from generation to generation in a precise and orderly fashion indicative of a mechanism, the workings of which can be revealed and the results of the workings of which can be predicted. If generation after generation of a family is in its turn exposed to the impress of environmental agencies which prevent development and induce deterioration, then any unhelpful quality exhibited cannot be said to be inherited, but if, in spite of the replacement of this deleterious environment by

another known to provoke fuller expression and betterment, such a character as feeble-mindedness still appears among the offspring generation after generation, then it can indeed be stated that the condition is the expression of an inborn difference which distinguishes its possessors from the rest of the stock. Thus, for example, many pedigrees are notable for the prevalence of suicide. Suicide, of course, is not inherited. It may be that individuals who happen to be related are in their turn overwhelmed by circumstances and that coincidence and not organic inheritance is responsible. But there is strong presumptive evidence which shows that suicide in such family is a form of expression of melancholia which is genetic in nature.

It is necessary to recognise clearly that the feeble-minded do not compete successfully with ordinary people and do not manage their affairs with ordinary prudence, not because they do not choose to do these things but because they cannot. It must be recognised also that every feeble-minded man is a potential drunkard, a potential criminal, that every feeble-minded woman is a potential prostitute and pauper, that all are destined to become the easy victims of their environment, because they are incapable of self-control, will-power, and of judgment, which alone enable mankind to control his environment. They are left unarmed to struggle vainly against the force that is older than love, the urge of sexual necessity.

Such as are feeble-minded as a result of accident or disease are to be regarded as good stock damaged by circumstances of their social environment, and one would not, without question, expect them to transmit the effects of this damage to their offspring. It should be noted, however, that the accidental or developmental feeble-minded are likely to be more frequent in stocks which are bad in other respects, since many of the causes of developmental feeble-mindedness (alcoholism, drugs, lack of prenatal care, and so forth) operate with greater severity among groups

with other hereditary stigmata, either mental or physical. Hence it is necessary to weed out all hereditary stigmata if feeble-mindedness is to be obliterated.

Such as are feeble-minded in virtue of their organic inheritance are to be looked upon as bad stock, for they will "breed true" to their character. But since as yet it is impossible, owing to the present inadequate and faulty methods of investigation, and because of the lack of reliable family histories, accurately and confidently to distinguish between the two kinds, the acquired and the inborn, it is necessary for the community to treat both as one class. The only acid test now available is controlled mating and this is impracticable. No doubt as knowledge increases and as the social environment is improved, it will become possible to distinguish between the two kinds, but to-day most attention must be given to the condition and not to the cause, for the matter is urgent. To rid a garden of weeds one plucks these out and steadfastly tills the soil in order that weeds may not grow. In the human garden it is necessary to pluck out the weeds in order to prevent their spread and steadfastly to develop the social environment in order that ultimately weeds will not appear.

The ranks of the physicians are closed and the forces are arranged. The battle is between those who hold that feeble-mindedness can be truly inherited and those who hold that it cannot, and whilst they fight the feeble-minded reproduce their kind. It is unreasonable to look for utter accuracy in the records of the feeble-minded: it is criminally foolish to wait for certainty before formulating policies and exerting control. It is a matter of very little importance, relatively, the question as to the exact mode of transmission of this character feeble-mindedness. If it is inherited at all, then in the light of our present knowledge concerning inheritance, it is essential, if it is desired that they shall not increase, that the feeble-minded shall not be allowed to reproduce their kind.

That the appearance of feeble-mindedness is in a multitude of cases definitely an instance of the transmission of this character from one generation to another is beyond reasonable doubt. Its incidence in family records points to the conclusion that it is most commonly of the nature of a recessive character.

If this is so, then it becomes an easy matter to identify, segregate, and even sterilise the feeble-minded, and thus prevent their multiplication, but it is an infinitely more difficult task to identify the carrier who, though apparently quite normal, will produce, when marrying a carrier or a feeble-minded person, a proportion of feeble-minded offspring. Until some method of identification of the carrier has been devised and perfected, then manifestly it remains desirable to encourage celibacy and chastity on the part of all the near relatives of a feeble-minded person.

At the present time the community is surely justified in basing its attitude towards feeble-mindedness on the assumption that it is a simple recessive character. The point of view of the State can become modified as knowledge increases, but the State cannot wait until everything is known before tackling, by legislation, this urgent problem of weeding the human garden. The surgeon operates not only to cure but incidentally to confirm his diagnosis of the cause of the trouble. There can be no doubt that as knowledge increases, this simple interpretation of the mode of inheritance of feeble-mindedness will become more and more modified, for the different grades of feeble-mindedness suggest a multiple series of hereditary conditions similar to those known in the case of laboratory animals, but this will not affect in any fundamental way the methods of eradication of feeble-mindedness from a population. There can be no doubt also that refinement in educational technique will invoke a greater development on the part of the feeble-minded and will allow these to approach more nearly the present standards of the normal stock. But the difference

will always exist and indeed become more pronounced if at the same time the methods of education applied to the normal are equally developed. No one, normal or abnormal, is yet able to achieve full expression of inborn potentialities.

The application of established biological principles to the case of the feeble-minded, if it be granted that in many cases feeble-mindedness is a true inborn character, would encourage the following policy:—

1. The feeble-minded must not be allowed to marry the feeble-minded.
2. A possible carrier should not marry into a family in which there is any history of feeble-mindedness.
3. Paupers, criminals, habitual drunkards, vagrants, prostitutes should be examined carefully and scientifically in order that the victims of circumstance might be separated from the victims of organic inheritance and treated differentially.
4. The feeble-minded should be segregated.
5. Sterilisation should be considered. It is a simple matter to render a person incapable of procreating: it is more difficult to prevent such a feeble-minded person, at liberty, spreading venereal diseases. The difficulty arises in the fact that sexual libido is not extinguished by such operative interference.

If feeble-mindedness is a recessive character, then segregation and sterilisation of the feeble-minded generation after generation will certainly reduce the proportion of feeble-minded in a population. But the process will be dreadfully slow. It has been estimated that to reduce the proportion from 1 per 1000 to 1 per 10,000 would require 68 generations, from 1 per 10,000 to 1 per 100,000 would require 216 generations, and from 1 per 100,000 to 1 in a million 684 generations. If this is not sufficiently fast, then the State must see to it that not only shall the feeble-minded not reproduce but also that no relative of a feeble-

minded person shall beget offspring. These figures must at once provoke a misapprehension concerning the effectiveness of selection in this matter of removing feeble-minded stocks from the population. If they are correct, it would indeed seem that the benefits of segregation and of sterilisation must be so tardy as to make elimination by such means unworthy of much consideration. But it has been shown that this method of presentation of the figures fails to convey the correct impression and that if the frequency of feeble-mindedness is expressed as so many per 10,000 the effects of such elimination on the immediate progeny can be demonstrated clearly. Elimination by segregation and/or sterilisation of all genetically feeble-minded, so that they could not reproduce, would lead to a reduction from 100 per 10,000 to 82·6 in a generation, from 82·6 to 69·4, and from 69·4 to 59·2, *i.e.* a reduction of 17 per cent. in a single generation and a permanent legacy of improved germ-plasm. It is desirable to repeat that these calculations are based upon two assumptions. It is assumed that the defect is a simple Mendelian recessive character, differing from normality by a single factor, and that individuals within a population choose their mates at random. This second assumption is open to serious criticism, for mating is not at random, being largely controlled by social class. The feeble-minded tend to gravitate to the lowest social stratum. It is recognised, moreover, that within each class like tends to consort with like—the feeble-minded tend to mate with feeble-minded. Such concentration renders the effects of segregation more certain and more rapid.

Much has been said of the endowment of marriages of the socially desirable; if such schemes are reasonable, then much remains to be said of the endowment of celibacy on the part of the bearers of unsound germ-plasm. One generation would be meting out fair treatment to its successors, were it to make it ethically admirable and, if necessary, financially advantageous for those who should not reproduce to abstain therefrom.

A new gene arises out of the old and replaces it, and the total number of genes remains unchanged. As to the exact nature of the change, nothing yet is known: for the present, it is sufficient to hold that any kind of change in a locus may yield a new characterisation. Nor is much known concerning the cause of mutation, concerning the origin of a gene. Since, however, the gene is regarded as chemico-physical in nature, it is reasonable to assume that mutation can be, and is, caused by physico-chemical agencies. It can be assumed that mutation does not occur in the absence of a sufficient cause and that this cause commonly is the action of an environmental factor. Chronic poisoning with alcohol, in non-lethal and non-sterilising doses, for example, may be expected to predispose the germ-plasm towards mutation. Such a disturbance would be of parakinetic origin if the germ-cells of the fœtus were damaged by the drinking habit of the pregnant mother, and idiokinetic in the case of the damaging of the germinal tissue of the drinker himself or herself. Other possible agencies provoking mutation are lead, mercury, nicotine, carbon, bisulphide, benzol, aniline, iodine, arsenic, X-rays and radio-active substances.

Such observations as have been made seem to show that the character of the mutation depends less upon the kind of idiokinetic agent than upon the nature of the germ-plasm itself. Mutations leading to severe disturbances and disharmony are relatively of little importance to the race, because their very severity prevents their reproduction. It is the multitude of relatively innocuous recessives that constitute the real problem in the spread of the unaffected carrier and the inevitable increase in the extracted homozygous type. Without careful and continuous selection, race degeneracy is eminently possible and even probable.

Though there are indications that the precision of the chromosome mechanism becomes somewhat affected with the age of the individual, there is no real evidence which shows that the characterisation of the offspring is affected

by the age of the parents. Most of the differences exhibited by children born of over-young and over-old parents respectively, are to be explained simply as the results of differences in nurture. It is not the age of the parent but the general physiological condition which can affect the developmental processes of the offspring. It may be expected that a "fit" mother, a happy mother, will give birth to a more physiologically harmonious child than will an unfit or distressed mother: that the spermatozoa of a "fit" man will be more functionally perfect than those of a diseased, immature, or senile man, but it is the general metabolic qualities that are affected, and not the genes themselves. There is no critical genetic evidence which supports the suggestion that the first-born is the inferior. Since there are more first-born than others in the general population, since diseased parents commonly have but few children, and since degeneracy is exhibited by the first-born before the others of the family are old enough to exhibit it, it follows that it would appear that there is this inferiority of the first-born. But the evidence is anecdotal and uncritical.

The popular views that telegony occurs and that maternal impression is responsible for the appearance of unusual characters find no support in critical experimentation.

CHAPTER VIII

CONCERNING DISEASE RESISTANCE AND NATURAL IMMUNITY

DISEASE of bacillary or bacterial origin is but the manifestation of the battle which is fought between the invading organism and the living body of the attacked. If the invader is immediately disarmed or repelled, no signs of a struggle will be evidenced: if the invader secures a foothold, then disharmony of one or more functions of the host is to be noted, and a definite train of signs and symptoms presents itself. If and when the defensive mechanisms of the body of the host overcome the activities of the invader, repair and recovery set in, but in many instances the battle is drawn, a compromise is effected between parasite and host, and the latter becomes a carrier, exhibiting few or no signs and symptoms of ill-health, but being continuously infected. The invader seeks victory, which commonly involves the death of the host, not only by a simple increase in numbers, but also by actively adjusting itself to withstand the mobilised defensive forces of the host. Modifications of pathogenic organisms are to be looked upon as the morphological reflections of physiological adaptation on the part of the organism in relation to a particular kind of unfavourable environment, such adaptations being commonly of the nature of intensified virulence, capsule formation and acquired resistance to particular therapeutic drugs.

That individuals differ among themselves in respect of their records of diseases is manifest, and evidence has already been considered which shows clearly that fundamental genetic dissimilarity, yielding differences in general physiological

constitution, can account for much of this. The problem now being considered is whether or not species and races are characterised by differences in their susceptibility to and immunity from disease. It is known that the guinea-pig and mouse are highly susceptible to infection with anthrax, rabbits less so, and the rat almost immune. The white mouse is said to be immune to glanders, the house mouse somewhat susceptible, and the field mouse highly susceptible. *Anopheles punctipennis* is not infected by the malarial parasite, *Anopheles maculipennis* most certainly is. The Algerian sheep is far less susceptible to anthrax than is the European sheep. The human is immune to many infections prevalent among his domesticated animals, and these to many of the infections of man. The negro is said to enjoy an immunity from yellow fever, the Mongolian from scarlet fever; the European, it is said, is relatively highly susceptible to yellow fever, diphtheria, and intestinal diseases such as cholera, dysentery, and typhoid, whereas the darker skinned races are held to be more prone to tuberculosis and other respiratory diseases, elephantiasis, and leprosy. The natives of any endemic area are supposed to be relatively immune from the particular disease of that area. The question which must be considered is whether or not these differences exist in fact, and, if so, whether or not they are expressions of genetic dissimilarities. Undoubtedly, susceptibility and resistance towards any particular disease vary within fairly wide limits, are seldom absolute, and have no relation to biological relationship.

Both the cellular and fluid elements of the blood play their parts in the defensive mechanism of the host. The white cells attack and digest the invading organisms, whilst in the serum are developed antibodies, bacteriocidins, agglutinins, lysins, anti-aggressinins, and the like, which destroy, immobilise, clump, and dissolve the organisms. The presence of antibodies in the serum, however, is not the only criterion of disease resistance, of relative or absolute

immunity, for the body cells themselves play a prominent rôle in ensuring the efficacy of the defensive mechanism, and in many cases, antibodies occurring in the absence of a definite attack of a pathogenic organism, are present only to a limited extent.

Natural immunity may be due to one of several causes. The entrance of the organism into the host's body may be prevented by the integrity of the skin and mucous membranes; the invader may at once be disarmed by the activity of enzymes in the skin or by the chemical and physical action of such secretions as the saliva or the gastric and intestinal juices. The organism may be repelled or embarrassed by the movement of cilia. Even though the organism gains entrance, it may be harmless if the particular route of infection required by the organism has not been followed or is not available. Certain tissues confer a marked local immunity to certain organisms, for example in the case of human diphtheria the infection very seldom proceeds along the œsophagus. The age of the host influences the conflict, as is seen in the case of ringworm for example, which is a disease of children under seven years of age particularly. The physiological constitution of the host is responsible for differences also, since the decision concerning infectivity is made by the ability or otherwise of the individual to mobilise blood quickly at the site of attack. Constitutional or transient differences in the activity of the leucocytes can account for differences in disease resistance. In certain cases, in tetanus for example, the organism requires suitable receptors in the body cells of the host before it can become pathogenic. Tetanus toxin, being unbound by the cells, produces no effect upon the turtle and antitoxin is not elaborated. In the case of the alligator, though the toxin is bound, no harmful effects follow because the body cells are not susceptible to the action of the parasite or of its products. The turtle and the alligator are both naturally immune from tetanus, though

for different reasons. In other instances, the natural immunity is not due to the bactericidal properties of the serum or leucocytes nor to antitoxins, but to the presence of substances, the so-called anti-aggressinins, which prevent the micro-organism from exercising its particular aggressive force. In still other cases the natural immunity is due to the fact that in a particular host the parasite fails to find adequate and appropriate nutriment. Such athreptic immunity may perhaps explain the failure of growth on the part of a tumour transplanted from one species to another. Certain organisms are known to require human protein for their well-being and so are restricted to man.

It is established that this specific and racial natural immunity is a reality. Two different opinions have been advanced to account for it. According to one view, when the pathogenic organism is first introduced to a population, all susceptible individuals—and this means most of the population — become infected, whilst a few, the relatively highly resistant or immune in virtue of their genetic constitutions, will remain unattacked. The population is thus passed through the sieve of selection. Such as are unable successfully to withstand the attack succumb, and in so doing remove themselves from the list of parents of the next generation. Since this next generation arises from the survivors, it will tend to inherit the natural immunity exhibited by its parents. Succeeding generations in their turn are exposed to the same infection until only those who can, for genetic reasons, pass through unscathed are left. The population ultimately consists solely of the descendants of those who possessed a complete or partial natural immunity. Disease resistance from this point of view is not attributable to any immunity acquired by such individuals as, contracting the disease, recover. The second view is that when a disease is first introduced into a population, all individuals are liable to contract it. Some perish and some recover, the result depending mainly upon the severity of infection in different

cases. Such as recover, in virtue of the exercise of their defensive mechanisms, have acquired a degree of immunity which persists to protect the individual from further attack and which is transmitted in some degree to the offspring, so that these, when in turn they contract the disease, are enabled to develop a still greater resistance. So, generation after generation, the acquisition is augmented until a specific immunity characterises the population. This hypothesis, which clearly involves the suggestion that acquired characters are truly heritable, is regarded by most present-day biologists as probably untenable in the light of our knowledge of the origin of the germ-cells, the behaviour of the hereditary characters, and the apparent lack of relation between such mutations as do occur and any discernible causal agency. There is no doubt that antibodies and such-like can be communicated from parent to offspring, but in such cases it is clear that the hereditary mechanism is not involved, for the immunised male parent cannot transmit its immunity.

Evidence is slowly accumulating which tends to show that immunities, like susceptibilities, are transmitted as genetic characters, taking the form of antibodies in the blood. The mode of inheritance of blood complement in the guinea-pig has been studied by the usual hybridisation methods of genetics. Crosses between strains in which the complement was deficient and normals gave results which showed that the character known as complement was inherited in a manner entirely in conformity with genetic laws. The complement-deficient strains were highly susceptible to disease and ultimately died out from this cause. In the guinea-pig too it has been shown in connection with the inbreeding work to which reference has been made, that the different inbred lines exhibited marked differences with respect to disease resistance, and that the character high resistance was transmitted in an orderly fashion by males and females of the lines exhibiting this character.

There is one record which shows very clearly indeed how

different races react differently to infection. A colony of mice, including Japanese, albinos and hybrids between these, were attacked by a virulent staphylococcal infection. All the Japanese were wiped out, whereas none of the albinos were affected nor were any of the F_1 hybrids. Of the F_2 individuals three in every four survived, of the back-crosses of F_1 and Japanese approximately 50 per cent. survived, and of the reciprocal back-crosses only one out of fifty-one died. These results agree with the assumption that susceptibility and resistance in this case constitute a single factor pair, that resistance is the dominant member of the pair and that the original Japanese were duplex for the susceptibility factor, the albinos duplex for the resistance factor.

In the case of the rabbit it has been shown that the subjecting of successive generations to typhoid inoculation led to the development of considerably higher agglutination titres in individuals out of lines which had been treated for three or four generations than in the case of the first generation of animals of untreated stock. It was noted, however, that whilst in successive months there was, with more or less fluctuation, a gradual lowering in the titre of the offspring of untreated mothers, almost invariably a decided spontaneous increase in the titre occurred in such young during the 5th to 6th month after birth. It was shown that the antibodies passed from mother to offspring via the placenta, and that the young of immunised mothers could, without further immunisation, transmit agglutinability to their own offspring. Such experimentation as this may be expected to define exactly differences between the communication and the transmission of immunities. In the case of the human the problem of natural immunity is very obscure. Yet it is one of the greatest importance, for upon it is based the problem of racial extension and colonisation of habitats differing widely one from the other in the matter of climate and fauna. A true racial immunity can only be recognised when, other things being equal, two races are living under

conditions to which each has already become adapted. The recognition of such immunity is made most difficult, however by differences in racial habits.

The case of osteomalacia may be cited as an example of this. This disease is comparatively very prevalent in the Punjab among certain Hindoo castes and the Borah Mahommedans of the Central Provinces, and in Western India. At first sight it would seem that these communities were genetically so constituted that proneness to osteomalacia was a distinguishing character. But when it is disclosed that among these communities purdah-nishin, with its sedentary seclusion and its unsanitary associations, is the rule, it becomes clear that habits and not genetics are at the root of the difference. Beri-beri is common among the peoples of the East Indies, China, Japan, and Malay, and rare elsewhere, but this is not due to any racial peculiarity but to the fact that these peoples eat such foods as polished rice. A people isolated by physiographical, religious, or social barriers will tend to show peculiarities in its diseases since infections of certain kinds may never reach them. It does not follow that because a disease disappears a people have attained an immunity: improvements in hygiene, public and personal, can account for this. Cholera, typhoid, and such like diseases are rare in Europe, but not because the European is immune thereto. Meteorological agencies play a most important rôle in the causation of disease: they affect the insect hosts of many diseases, governing their habits and distribution; they affect also the pathogenic organism undergoing one part of its life cycle in an insect host in those cases in which such development is conditioned by temperature and humidity. Depressing climatic conditions in lowering the vitality of the human, rendering him less able to withstand the attacks of pathogenic organisms, also play their part.

The suggestion that the negro contracts yellow fever less readily than does the white is not confirmed by really

critical observation, though it would indeed seem to be established that the death-rate from this disease is much lower among negroes than among infected whites. The apparent immunity to malaria exhibited by peoples living in malarial districts is to be explained as the result of an acquired tolerance. The greater the intensity of the infection, the earlier in life will the community be infected and at the time of maturity all who have survived will have acquired tolerance. It is not yet demonstrated that by this means a more resistant race is evolved. That the European is more liable to intestinal disorders in India than the native is probably to be explained on the assumption that the European is at the mercy of his native servants and that his illness is always recorded.

It is now generally accepted that a relative immunity to tuberculosis does exist in certain races, but the usual explanation of this fact is that the relative incidence of the disease is nothing more than a reflection of antecedent contact with the disease. The negro and other less highly organised peoples are highly susceptible to this infection. The long industrialised community is relatively free. Surveys, in which modern tuberculin tests were made, have shown, however, that the difference between peoples is exactly the same as that between urban and rural communities. The civilised peoples and the urban populations show a high morbidity and a low mortality, whereas the non-industrialised peoples and the rural communities exhibit a low morbidity but a very high mortality, the disease occurring among them in its most acute form. Figures showing the incidence by nationalities per 1000 men during a twelvemonth among the French Army of Occupation (Lasnet and Treband) are of interest in this connection—

Senegalese	86·07	Arabs	13·33
Malgaches	18·88	Moroccans	11·73
Annamites	15·31	French	9·55

There is no reason to hold that these differences are indications of genetic dissimilarity, although in the matter of susceptibility to tuberculosis it may be that they are in respect of general physiological characterisation. It is sufficient to regard them as the result of differences in previous exposure to the disease.

The application of the Schick test to populations seems to show that in the case of diphtheria the incidence of the disease is determined by the extent of the opportunities for contracting the disease and not by any special natural immunity. The reputed immunity of the Mongolian to scarlet fever does not appear to exist in fact. It would appear to be the case that this disease is more prevalent and virulent in Northern than in Southern China, but this difference cannot be related to any genetic difference between the peoples. There is no critical evidence which supports the contention that the white is less susceptible to leprosy than is the coloured, or that an admixture of dark blood increases the liability to contract leprosy and elephantiasis. Such racial differences are to be explained as indications of differences in sanitation and habits.

Until recently it has not been possible to discuss at all satisfactorily the question as to whether or not organic inheritance played any part in the incidence of cancer. Plentiful statistical studies have been made concerning the incidence of cancer in populations, but these have yielded contradictory results as they were bound to do because of the errors inherent in the data obtained from such sources. All such statistical evidence must be valueless until post-mortem examination has become exact. Such statistics as do exist can be used to show that cancerous patients have more cancerous relations than have patients suffering from other diseases, or on the other hand to show that they do not. The prejudiced can make their choice. Much attention has been paid to the occurrence of families in which a strikingly large proportion of members

are cancerous. Undoubtedly such cancer families exist: the Bonaparte family, for example, in which Napoleon, his father, his brother Lucien, and two of his sisters, Pauline and Caroline, are all reported as having died of cancer of the stomach. But family tradition and belief, incomplete recording, inexact diagnosis, must remove much of the value of these records. Even though family history after family history is added to the list, the possibility that the concentration of cancer in families may still depend on chance alone and not be an indication of the heritability of cancer must be considered. If 10 per cent. of a population over forty years of age become cancerous, then chance may leave some families free and others will be crowded with cancerous individuals. But if a peculiar type of tumour or a peculiar site of tumour growth is considered, and if records show that either of these characterises members within a family and in successive generations, then the laws of chance become inadequate to explain the facts. Glioma of the retina is rare; it occurs in infants and its familial incidence is remarkable. Melanosarcoma of the choroid of the left eye is recorded in a grandfather, a mother and her two sisters, and in a daughter. Twin sisters have developed a fibroadenoma of the left breast, each of the same microscopic structure, occurring at the same age and in the same site. In one family all members who were not twins died from cancer, all the twins escaping. Of the 48 descendants of a cancerous grandfather, 17 died from cancer (10 carcinoma of uterus and 7 carcinoma of the stomach). There is no escape from the conclusion that a definite and marked susceptibility to cancer exists in certain families, being most pronounced in cases in which there is a cancerous history in both paternal and maternal lines. In these cases the tendency seems to be for the disease to appear earlier and to be more malignant.

To such as incline to the view that neoplasms have their origin in embryonic rests, there is no difficulty in visualising

the hereditary nature of the condition. But even to those who prefer the newer views, there can be no insurmountable difficulty in this matter, for there is abundant evidence to show the reasonableness of postulating biochemical and biophysical differences having their origin in genetic dissimilarity.

There is no doubt concerning the inheritance of the tendency to develop benign tumours such as hereditary telangiectasis, multiple benign cystic epitheliomata, multiple cartilaginous exostoses, von Recklinghausen's disease (multiple neurofibromatosis), and so forth, which bear resemblances to carcinoma. The mechanism of heredity is certainly such as could provide for the inheritance of susceptibility or of resistance to cancer.

Tumour transplantation work has shown that close relationship of animals is favourable for success in inoculation, and that genetic differences determine success or failure in inoculation. It has shown also that certain strains of animals are insusceptible to tumour grafts to which other strains of the same species are susceptible. It has shown that organic inheritance influences in a constant manner the susceptibility of a given strain of animals to inoculation with cancer. Japanese waltzing mice are prone to develop a particular carcinoma which will not grow in certain strains of ordinary mice. The F_1 individuals between Japanese and ordinary mice are all susceptible. Further breeding showed that the susceptibility to grafted tumours in this case was based upon about 12 to 14 independently inherited factors. In other cases, in which different tumours and different mice were used, the results were different so that it is impossible to generalise in this matter. In rats also it has been shown that resistance and susceptibility to grafted tumours are to be regarded as genetic characters though in most cases multifactor in nature. The possibility that the tendency to develop spontaneous tumours is hereditary has also been studied, and the conclusion, in one case in

the mouse, was reached that the data indicated that one of the factors in the development of tumours is to be found in an inherited character or peculiarity. In another experiment the fact emerged clearly that the type and site of spontaneous tumours were influenced by the forces of heredity, whilst in yet another it was concluded that organic inheritance played an important rôle in determining the incidence of a particular subcutaneous cancer of the mouse, since strains could be established which showed an almost constant proportion of cancerous individuals (58 to 65 per cent.) for several generations. The tendency on the part of the individual to develop tumours depends upon many factors which determine the intensity of growth of the tumour. The greater the tendency the earlier will the tumour appear and the greater will be the probability that in related individuals there will be a tendency to develop tumours.

The most ambitious genetical study of the influence of organic inheritance on the incidence of tumours in the mouse dealt with over 40,000 individuals and was continued for more than twelve years. The breeding system was carefully planned with stocks in which cancer is common, rare, and non-existent. No artificial influence known to affect the life processes of the mouse was allowed to operate during the course of the experiment. Epidemics were anticipated and the colonies were maintained under the best-known conditions. All individuals were post-mortemed and some 5000 spontaneous tumours, mostly malignant, were observed. From this most critical experimentation the following conclusions were reached. Cancer in the mouse appears in most of the forms encountered in man; mammary carcinoma, papillary adenomata, and carcinomata of the lung, primary liver tumours, sarcomata, squamous carcinoma of the skin and mouth, testicular tumours, basal-cell carcinoma of the head, squamous carcinoma of the stomach, papillary adenoma of the ovary, primary renal and suprarenal tumours, leiomyomata of the uterus, were all encountered.

The tendency to develop cancer or the capacity to resist cancer is unquestionably influenced by organic inheritance. Strains were developed in which not a single case of tumour development was seen for as many as thirty generations. In other strains cancer became so common as to be the sole cause of death of the individuals comprising them. The resistance to cancer in these mice behaved as a typical dominant character, proneness to develop cancer as a recessive. Cancer-developing and non-cancer-developing tendencies segregated as unit characters. Moreover, not only was the incidence of cancer influenced by organic inheritance but so also were the site and the character of the cancer. In certain strains the typical tumour was sarcoma, in others sarcoma was never encountered. In some strains the tumour was invariably mammary in its location, in others it was always hepatic, in yet another it was testicular. In the cow, it will be remembered that mammary neoplasms are extremely rare, hepatic and adrenal common; in swine the commonest tumour is embryonic adenosarcoma of the kidney; in rats sarcomata are more common than carcinomata; in the negro the uterine leiomyoma is exceedingly frequent.

The behaviour of the tumour was found to be influenced by organic inheritance, as was seen in the peculiar localisation of secondary tumour growths. Certain types of mammary neoplasms, for example, invariably led to pulmonary metastases in some strains, whereas in other strains they did not.

In the case of the rat it has been found that experimental infection with the tapeworm, *Tænia crassicollis*, is followed in certain strains but not in all by the development of sarcomata of the liver. By breeding together these susceptible rats, strains were developed in which all the individuals developed the sarcomata after infection.

In *Drosophila melanogaster* several cases of the inheritance of the tendency to develop tumours have been investigated.

One of the most interesting is that in which in a certain culture one-fourth of the larvæ developed masses of black pigment on the body; these larvæ were without exception males and invariably died. The growth consisted of a solid mass of large cells producing much pigment which resembled melanin. Since these tumours consisted of atypical cellular growths, invariably killed the individual they attacked, were transplantable, formed typical metastases, developed in embryonic rudiments, showed irregular mitotic figures, and since sterile eggs raised under aseptic conditions could still yield individuals exhibiting this tumour, it is not unreasonable to regard the tumour as a true malignant neoplasm resembling mammalian cancer.

In this case the tendency to develop tumours is a sex-linked recessive character. By mating up a stock carrying this sex-linked gene (t) and the genes for yellow body and white eye which are nearby in the X-chromosome, it is possible to distinguish between the normal and the carrier female since in the case of the offspring of the heterozygous female the tumour-bearing daughters will be grey-bodied and red-eyed whilst the non-tumour-bearing will be yellow and white as is shown in the following scheme:—

Yellow white normal ♂	(TywX)Y	×	(TywX)(tYWX)	Heterozygous grey red tumour ♀
(TywX)(TywX) yellow white non-tumour ♀	(TywX)(tYWX) grey red ♀ heterozygous for tumour		(TywX)Y yellow white ♂ (normal)	(tYWX)Y Grey red tumour ♂ (dies)

In this case it appears that under the ordinary conditions of development the tumour invariably appears: its appearance is not conditioned by any extrinsic circumstances incident to development. In the other instances the tumour is not developed in the absence of appropriate conditions, it is the liability to develop tumour under appropriate provocation that is transmitted.

The bearing of this experimental evidence upon the

problem of human cancer is clear. Cancer in the experimental animals is, in all essential respects, the same disease as cancer in the human. The fundamental laws of genetics apply to all forms, experimental animals and men alike. Many records of human cancer point to the conclusion that its mode of inheritance is the same as that which obtains in the case of cancer among experimental quickly-reproducing forms. Other characters, normal and abnormal, are inherited in a significantly orderly fashion in the human, and so there is every reason to hold that the human hereditary mechanism is the same as that which has been shown to exist in the experimental forms. The statistical data concerning cancer can be reconciled with the finding that the tendency to develop cancer is a genetic recessive character. It should be stated, however, that there are pedigrees in which carcinoma of the stomach behaves in inheritance as a dominant. The suggestion which emerges from these considerations is that particular attention should be paid to the recording of the family histories of individuals both of whose parents have suffered from cancer. Such histories must be supported by critical post-mortem findings. If, as seems probable, cancer in the human requires for its development an exciting cause, then not every individual possessing the necessary genetic basis for its development will become cancerous. This qualification must be noted when pedigrees are examined and prognosis made.

CHAPTER IX

CONCERNING THE IMPLICATIONS OF GENETIC FACT AND THEORY

THE basis of most of the present systems of government, education, ethics, and religion, is the conception that every man is the omnipotent architect of his own character; that he is as a clean slate upon which he himself may write what he chooses, unhindered by any kind of necessity, inborn or environmental, and that he is to be judged by what he has written of his own free will. Conduct, rational or irrational, benevolent or criminal, rests upon voluntary choice, and he who chooses to act otherwise than in accord with the tenets of the creed is held to be deliberately heretic and is punished.

But science has revealed the fact that natural phenomena are not the expressions of volitions on the part of beneficent or malevolent deities, but are the results of all the events that have preceded them. Nature is not the caprice of gods or of devils but an eternal process, ever moving on. Science recognises in everything the inevitable sequence of cause and effect, the universality of natural law. Man is a part of nature, a part of the great mechanism of the universe, and all that he is and all that he does is limited and prescribed by natural laws. Every step of his development has been, and is, determined by antecedent causes. One fact, clearly established, has emerged from the study of the phenomena of inheritance, viz., that in the main the future characterisation of the individual is predetermined in the fertilised egg in which the individual had its origin, by the contributions of the so-called germ-plasm received

by way of the egg and the sperm. The main characteristics—the characteristics of the species, of the race, of the family, and of the individual—of every living thing are unalterably fixed by organic inheritance. By the shuffle and deal of the hereditary factors during the formation of the reproductive cells of the parents and by the chance union of two of these cells in fertilisation, the hereditary constitution of the individual is for ever decided; all the possibilities of the individual are fixed. All men are not created free and equal, but handicapped and unequal. This is the doctrine of the biologist.

There are many who hold indeed that acts, habits, and character are foreordained and that men are not free to do this or that but that their reactions are predetermined by their inheritance. This attitude strikes fiercely at the opinion of those who believe ardently in the beneficent results of teaching and of democratic government, for it postulates that men are socially worthy or unworthy wholly in virtue of their organic inheritance; that the socially unworthy should not be pitied, and that all punishments should be visited upon the parents to the third and fourth generation.

One of the most difficult things in the world is to recognise a great truth, to appreciate its significance, and yet not to be carried away by it. Error in science is due to sweeping conclusion more often than to faulty observation. In philosophy, heinous errors are due not so much to false. premises as to supposed logical necessities. As a test of truth, logic is inferior to experience, and a logical chain has led many a man and many an organisation into the bondage of error.

In biology, the search for universal laws is a particularly dangerous pursuit. It is indeed easy and natural, when once the observation has been made that the main mental and bodily characters are determined by the mechanism of organic inheritance, to conclude that not only are all the

possibilities of human lives predetermined in the germ-plasm, but that also all the characters that will actually develop from the germ are there determined and cannot be altered. Such a conception of predetermination denies development altogether. It must not be forgotten that as far as the mind is concerned, there is no organic hereditary continuity with past and with future generations. Predetermination implies nothing more than that the development of a particular character or particular characters is made possible. Characters are potential and not actual in the fertilised egg, and their expression depends upon many complicated reactions of the elements of this hereditary constitution, one with another, and with their environment. Personality is not predetermined in the fertilised egg although its limits are certainly defined. The expression of the hereditary constitution of an individual is conditioned by its environment. Life is only possible within rather narrow limits of physical and chemical conditions, and, in the main, these are fixed by the constitution of nature. But within these limits is a multitude of minor environmental conditions which exercise a most profound influence upon the individual, especially during the period of development and growth. Food, temperature, moisture, and so forth, can produce profound changes in the developing individual under circumstances quite beyond the control of the individual affected. No individual can hope to express fully every quality with which he is endowed by organic inheritance: the potentialities of development are far greater than the actualities. Any character that can develop is potential and under given conditions of environment is predetermined, but, since the environment cannot be everything at once, many hereditary qualities must necessarily remain unexpressed. The results of development are not predetermined by organic inheritance alone but also by the fortuitous combination of extrinsic agencies.

Man, of all living things, enjoys the most varied environment, and the effect of this upon his personality is correspondingly great. He has a prolonged period of immaturity and it is during this period that the impress of environmental stimuli is most effective in modifying development. He develops amid a social inheritance, and intellectual, social, and moral stimuli play ceaselessly upon him: he lives in the past and in the future as well as in the present. The social inheritance can and does, in many a man, override his organic inheritance. Habits, thoughts, aspirations, ideals, responsibility, morality, religion, are contributions of the social environment and of education; chance, organic inheritance, and environment decide much of what an individual shall be, and there are hereditary limits to what a man may become, but these limits are not so narrow as is sometimes thought and within them a man has a considerable degree of freedom and of responsibility.

There is a still larger freedom and a greater responsibility than those pertaining to the individual. What the individual cannot do because of weakness, ignorance, self-interest, restricted life-span, society can accomplish with the strength, wisdom, and interest of all, and through long periods of time. The freedom, power, and responsibility of society are founded upon limitations of individual freedom for the good of the race. Among social animals, such as the ant or the bee, there is much instinct and little reason and freedom, and so there is no conflict between individual and society, but with the increase of intelligence and of freedom among men there has developed an increasing conflict between these. The perpetual struggle against social limitations that are artificial, selfish, for the good of the few, the struggle for freedom from tyranny in thought and speech in religion and government, is one of the greatest glories of the human. But all social restrictions on individual freedom are not artificial and selfish: some

are absolutely essential not only to the welfare but even to the continued existence of the race, and when demands for individual freedom clash with such racial obligations, they have to be regarded as a menace and dealt with accordingly.

Race-preservation, not self-preservation, has been the first law of nature and, among all organisms, the race is of paramount importance, its perpetuation and welfare being cared for by the strongest instincts. In many species reproduction means the death of the individual. Even among the higher organisms, the strongest of all the instincts are those connected with reproduction, but in the human, intellect and freedom interfere with instinct; the reproductive instinct is not only controlled by reason, as it should be, but is commonly also thwarted and perverted. If the demand for individual freedom blinds men to their racial obligations, then the decadence and extinction of their lines must inevitably follow. The best use a man can make of his freedom is to place limitations upon it. There must be law whilst there is inequality in spiritual and material possessions. Anarchy is the political creed of equals, biologically and socially, and the time for this is not yet.

The supreme duty of society is to weed out its worst qualities and to nurture its best. Racial improvement is to be achieved under conditions in which the physical and intellectual improvement of the individual does not interfere with his racial and ethical obligations and in which the promotion of human betterment is undertaken by society as its greatest work. Individual improvement is a necessary concomitant of racial betterment, and the first duty of the individual is to transmit unimpaired and undefiled a noble heritage to generations yet unborn.

It is eminently possible to improve the environment in which the individual and the race shall develop; it is eminently possible to improve education, making it a potent factor in development, so that the individual may discover

his powers and his limitations and recognise the ways by which he may achieve the fullest expression of his organic inheritance. It is possible to improve the organic inheritance of a people by negative eugenic measures, *i.e.*, by preventing the multiplication of stocks bearing defects, and by positive eugenic measures such as by cultivating the eugenic conscience which would insist that those who have a goodly organic inheritance should not practise voluntary infertility, by increasing opportunities for early and favourable marriages and by carefully conserving the best.

The streams that feed the torrent of defective and degenerate organic inheritance can be dammed by controlling marriage and immigration, by segregating and sterilising the serious defectives. Marriage biologically is an experiment in breeding; this being so, hereditary diseases should be regarded as a serious objection to marriage and a bar to reproduction. The law and respectability err grievously when they insist that, to save a woman's honour, sexual offenders must marry and thereby combine two streams of defective germ-plasm which shall flow on and on. A better way than that of constructing elaborate marriage laws is to educate public sentiment and to foster a popular eugenic conscience, for in the absence of this the safeguards of the law must for ever be largely without avail. Society being organised as it now is, to consider the financial consequences of marriage is praiseworthy caution, but it should be no more unromantic to examine a pedigree than a bank book. Though the idea of parenthood is not nowadays entertained seriously by many who wed, even in these cases children may be expected to present themselves, and a profitless scholar is a great burden to income.

Epileptics, idiots, and certain criminals who may become wards of the State could be segregated so that their organic inheritance would not escape to furnish additional burdens to society. A defective born may have the right to live and to enjoy whatever freedom is compatible with the

lives and freedom of the rest of society, but society surely has the right to protect itself against repetitions of hereditary blunders.

Confirmed criminals, imbeciles, and rapists could be sterilised. If this were done, there is reason to think that the prison and asylum population would diminish.

The enlargement of opportunity for the physically and mentally fit must not be embarrassed by philanthropic endeavour directed towards the alleviations of the conditions of the genetically unfit. The hospital must cease to be the hallmark of the civilisation of a community, and a city's pride must be its schools and gymnasia. Preventable waste such as war and the enforced celibacy of the socially worthy must be eradicated. Pride of family must be encouraged.

But who shall sit in judgment and separate fit from unfit? These are relative terms, and in their definition one must allow for differences in point of view. Before action is taken, it is essential that man shall know what is man and what man may become. If and when it is decided what kind of thing mankind shall become, if and when standards of merit have been constructed, then the biologist will be able to help in the achievement of these by indicating the most promising methods of approach. But the biologist alone is not competent to draw up these standards: neither is the enthusiastic amateur statesman whose only claim to note is his sincerity.

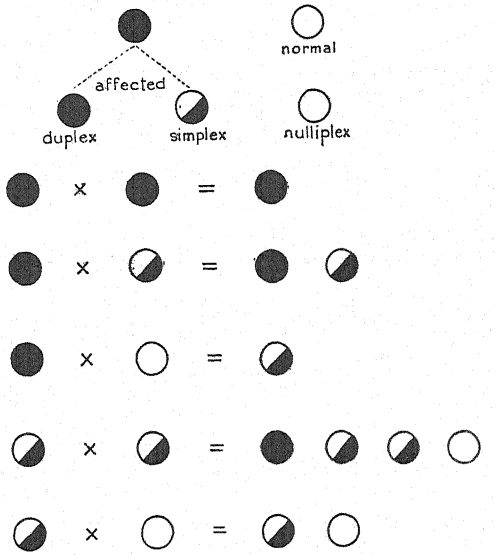
Those who make and mend the road along which mankind is travelling are wondering if they who lead really know where the road ends. Statescraft that is not in harmony with the facts of human biology, as these become disclosed, cannot possibly endure and indeed must do grave harm. The student of medicine who ceases to be a biologist with the close of the first year of his curriculum may later develop an extensive practice—this is not difficult—but he cannot hope to cultivate that which is of greater importance,

an appreciation of the fact that he of all men is an applied biologist.

"Bless not thyself that thou wert born in Athens, but among thy multiplied acknowledgments lift up one hand to Heaven that thou wert born of honest parents, that modesty, veracity, and humility lay in the same egg and came into the world with thee." This is a thought that could well form the basis of a new standard of social values.

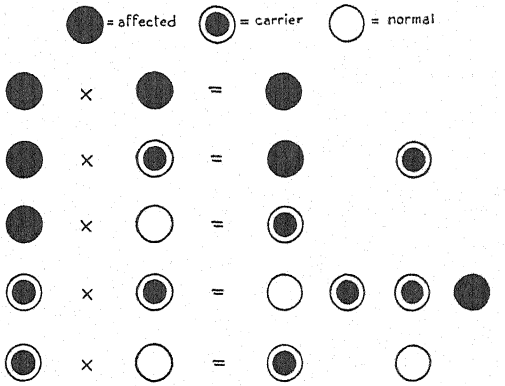
APPENDIX

THE MODE OF INHERITANCE OF A DOMINANT CHARACTER.



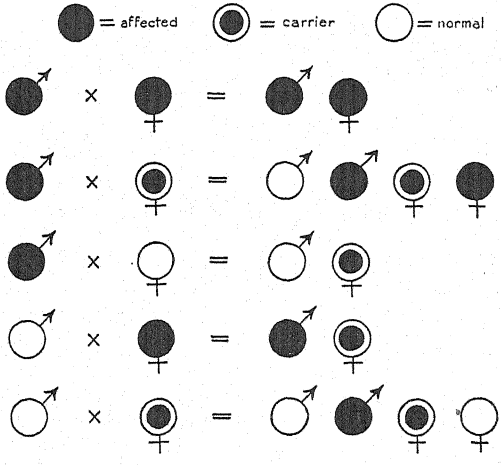
The character, being dominant, is exhibited by individuals either duplex or simplex for the factor concerned. The non-appearance of such a character in the offspring implies that either one or both parents were simplex for this factor, or else that one was simplex and the other nulliplex.

THE MODE OF INHERITANCE OF A RECESSIVE CHARACTER.



The character, being recessive, is exhibited only by such individuals as are duplex for the factor concerned. The individual simplex for this factor is apparently normal. The appearance of such a character in the offspring implies that (1) both parents were affected, (2) one was affected and the other was a carrier, or (3) both were carriers.

THE MODE OF INHERITANCE OF A SEX-LINKED CHARACTER.

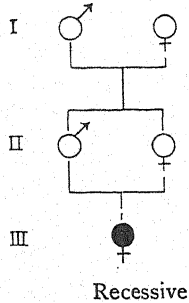


If the character is a dominant, then instead of "carrier" read "simplex" or "heterozygous," noting that such simplex individuals will exhibit the character.

EXAMPLES OF PEDIGREES SHOWING THE MODE OF INHERITANCE OF CERTAIN ABNORMALITIES.

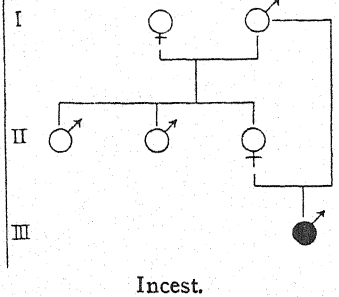
ALBINISM.

After BERNISS.



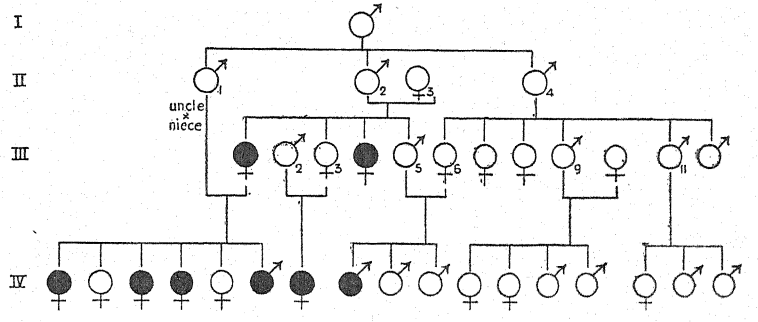
Recessive.

After PEARSON.



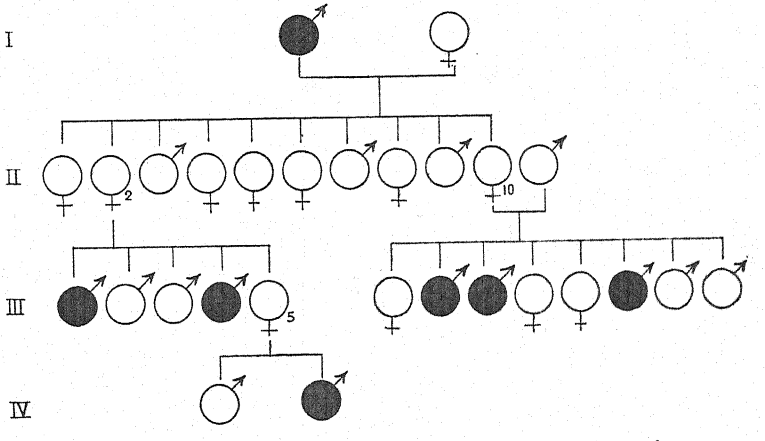
Incest.

ALBINISM. *After* TERTSCH.



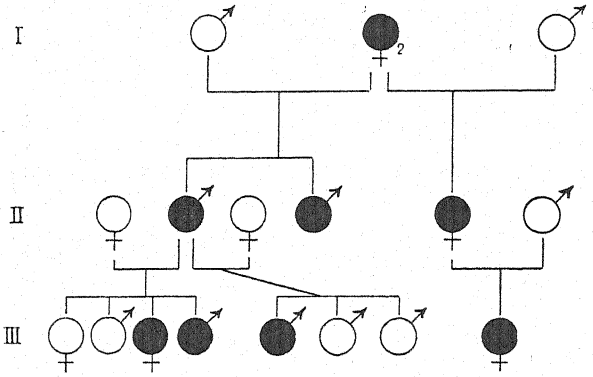
Recessive. Consanguinity. II, 1, 2, 3, 4, carriers. III, 2 and 3, 5 and 6, cousins. III, 9, 11, unaffected or carriers.

ALBINISM, LIMITED TO THE EYE, WITH NYSTAGMUS.
After MANSFIELD, abbreviated.



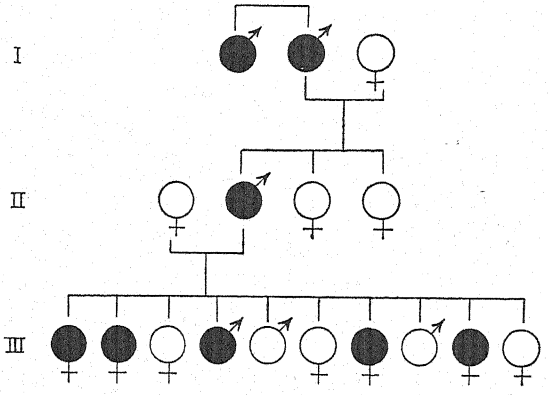
Recessive. Sex-linked. II, 2, 10, carriers. III, 5, carrier.

ANGIONEUROTIC ŒDEMA. *After* CAMERON.



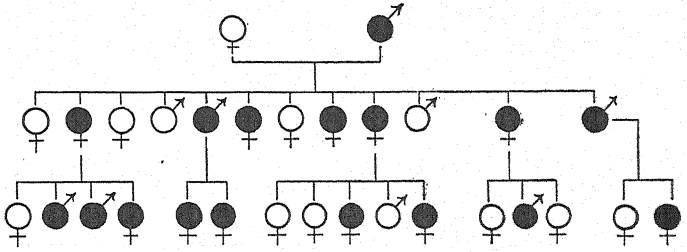
Dominant. I, 2, perhaps homozygous. II, III, all affected individuals, heterozygous.

ANIRIDIA. *After* CLAUSEN.



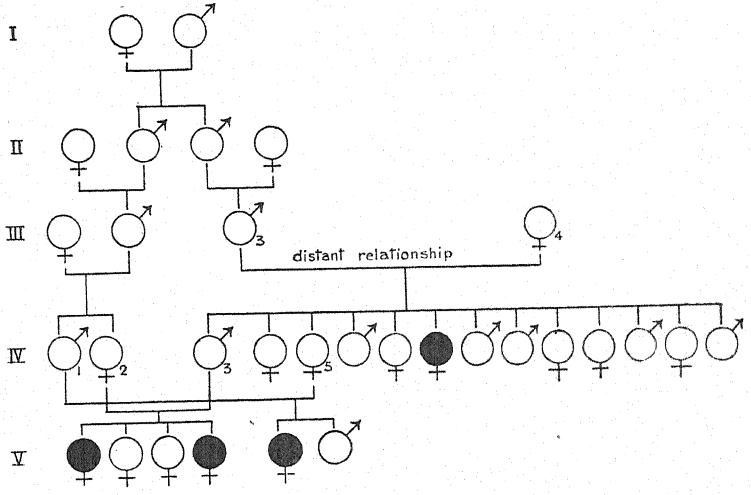
Dominant. All affected individuals are heterozygous.

BRACHYDACTYLY. *After* FARABEE, abbreviated.



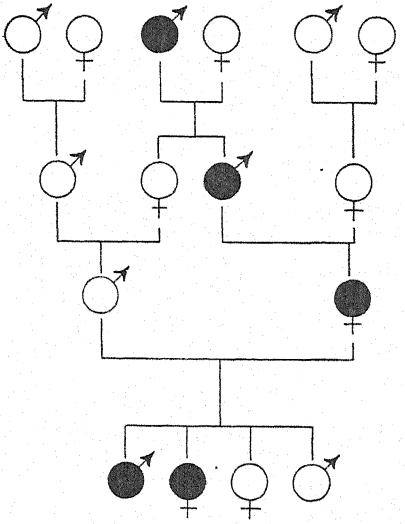
Dominant. All affected persons are heterozygous.

BULLOSIS CONNATA OR PEMPHIGUS CONNATUS.
After JENNY.



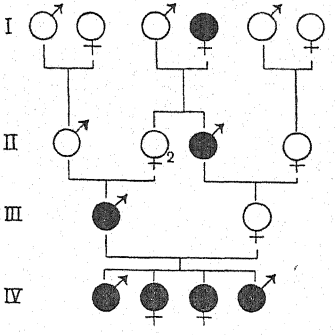
Recessive. Consanguinity. I, II, III, one or both of each pair must have been carriers. III, 3 and 4; IV, 1, 2, 3, 5, must also have been carriers.

CARCINOMA OF THE STOMACH. *After* GROTE.



Dominant. All affected individuals are heterozygous.

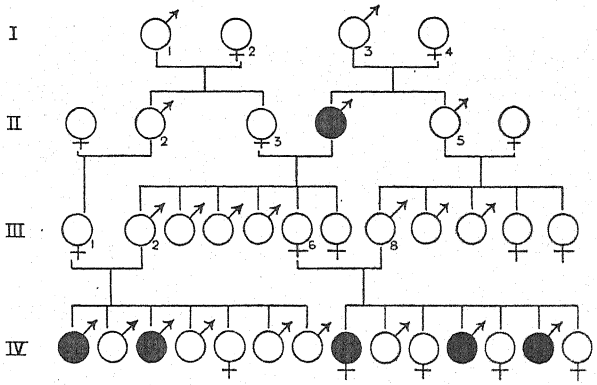
GREY CATARACT. *After* GROTE.



Dominant. Consanguinity. II, 2, perhaps died before cataract developed.

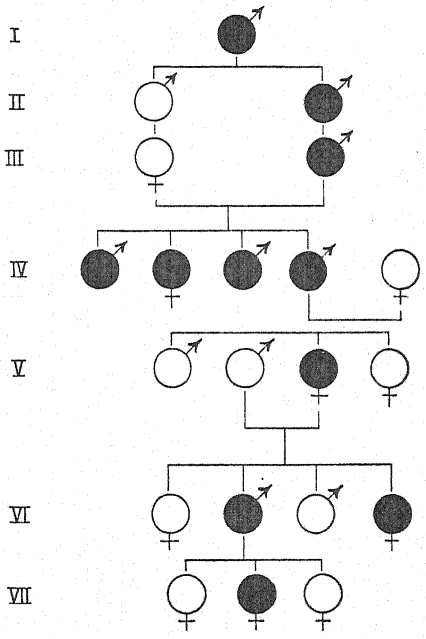
CHONDRODYSTROPHY (ACHONDROPLASIA).

After BONNEVIE.



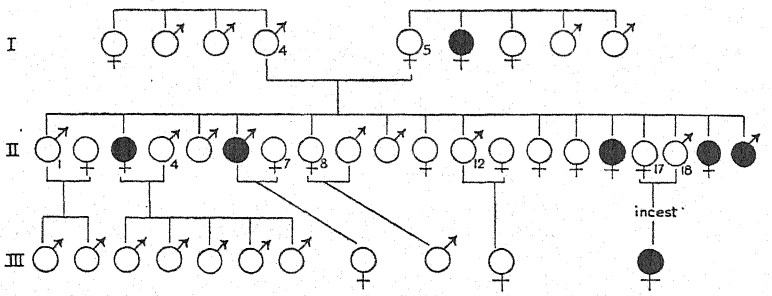
Recessive. I, 1 and/or 2, 3, 4, carriers. II, 2, 3, 5, carriers. III, 1, 2, cousins, also 6 and 8 cousins, and all carriers.

CHOREA. *After* ENTRES.



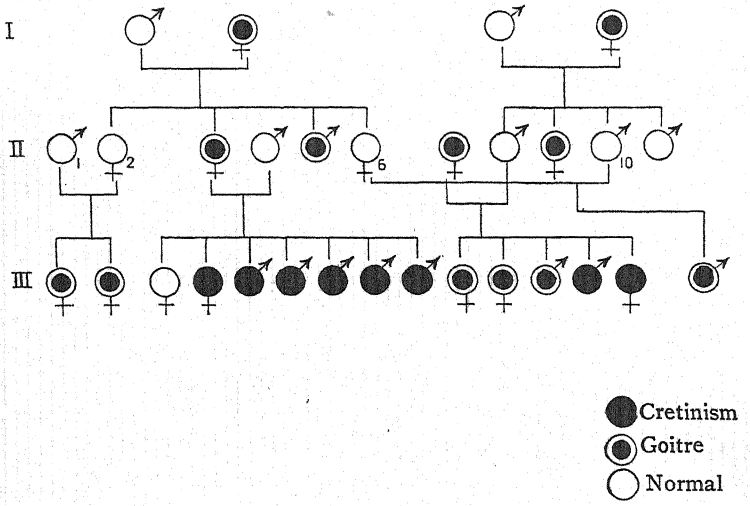
Dominant. All affected individuals are heterozygous.

CLUB-FOOT. *After* TETSCHER.



Recessive. I, 4 and/or 5, carriers. II, 4 and 7, carriers. II, 1, 8, 12, carriers or unaffected. II, 17 and 18, carriers.

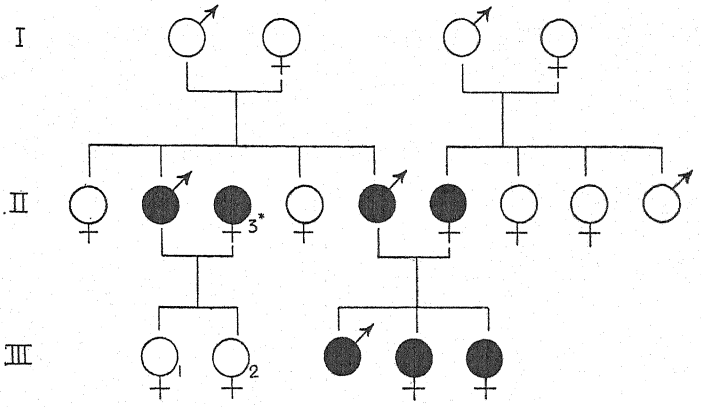
CRETINISM AND GOITRE. *After* PFAUNDLER.



Cretinism. All cretinous individuals have a goitrous mother.

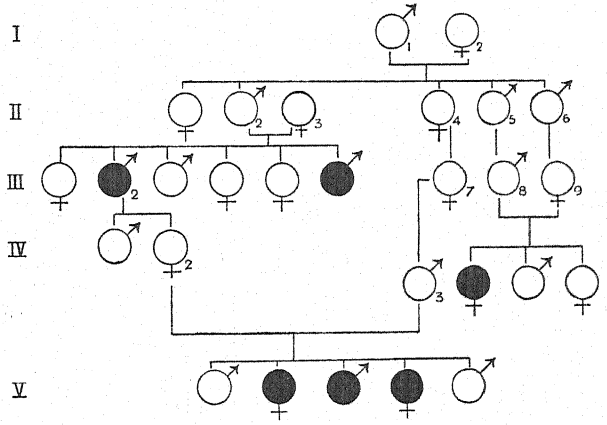
Goitre. Dominant, II, 2 and 6 are heterozygous, but do not exhibit the condition.

DEAF-MUTISM. *After* ALBRECHT.



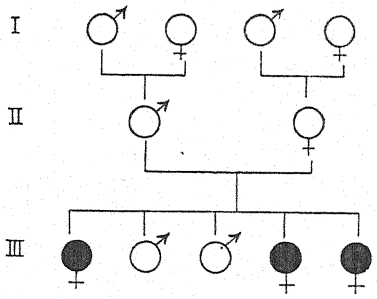
Recessive. I, all carriers. II, 3, non-hereditary deaf-mutism in consequence of scarlet fever; thus III, 1 and 2 are carriers.

DEAF-MUTISM. *After* ALBRECHT.



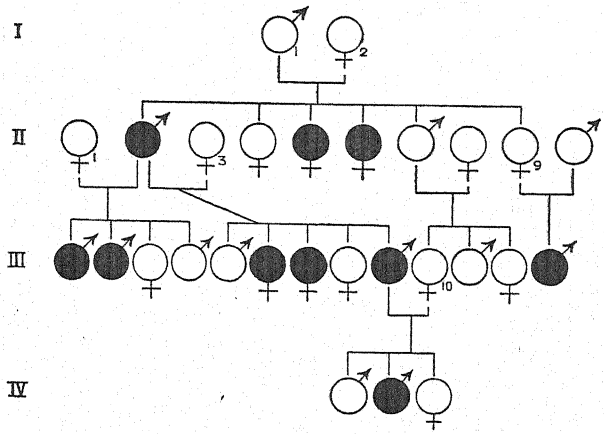
Recessive. Consanguinity. I, 1 and/or 2, carriers. II, 2, 3, 4, 5, 6, carriers. III, 2 must have married a normal woman. III, 7, 8, 9, carriers. IV, 2 and 3, carriers.

DEMENTIA AMAUROTICANS. *After* STARCK.



Recessive. Consanguinity. I, one member of each (at least) is a carrier. II, both carriers.

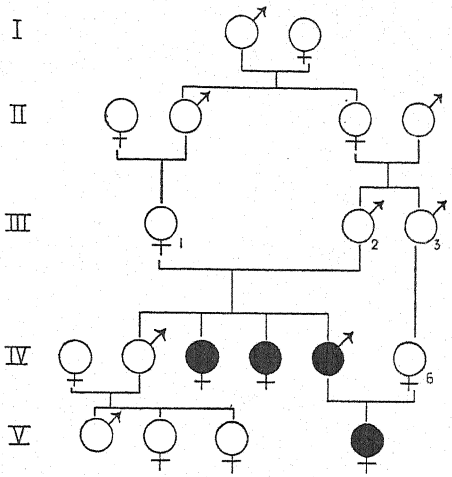
DIABETES. *After* HANSEN.



Recessive (irregular). I, 1 and 2; II, 1, 3, 9; III, 10, all carriers.

EPIDERMOLYSIS BULLOSA DYSTROPHICA.

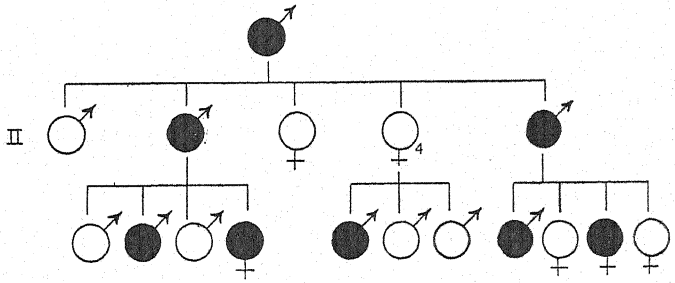
After SAKAGUCHI.



Recessive. Consanguinity. I, II, one member of each pair (at least) carriers. III, 1, 2, 3, carriers. IV, 6 is a carrier.

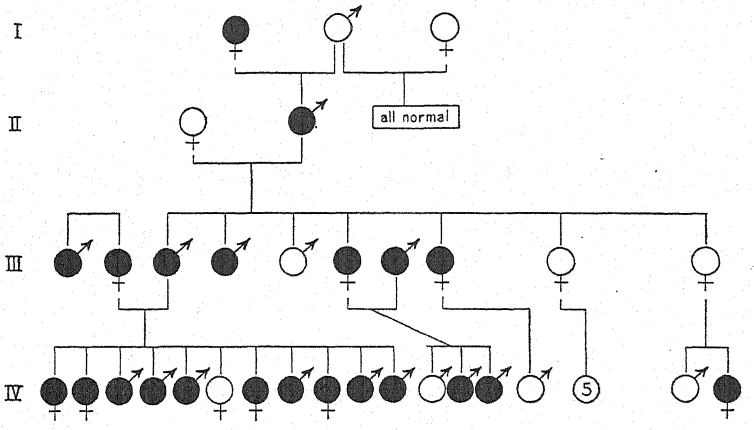
EPIDERMOLYSIS BULLOSA TRAUMATICA.

After COLOMBINI.



Dominant (irregular). All affected persons are heterozygous. III, 4 must carry the gene, although she does not exhibit the character.

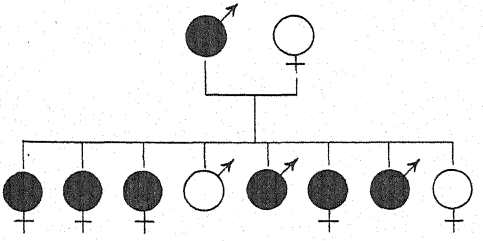
FEEBLE-MINDEDNESS. *After* GODDARD.



Dominant. All affected individuals in I, II, and III are heterozygous. IV, Expected ratio=25% homozygous, 50% heterozygous (=75% affected), and 25% normal.

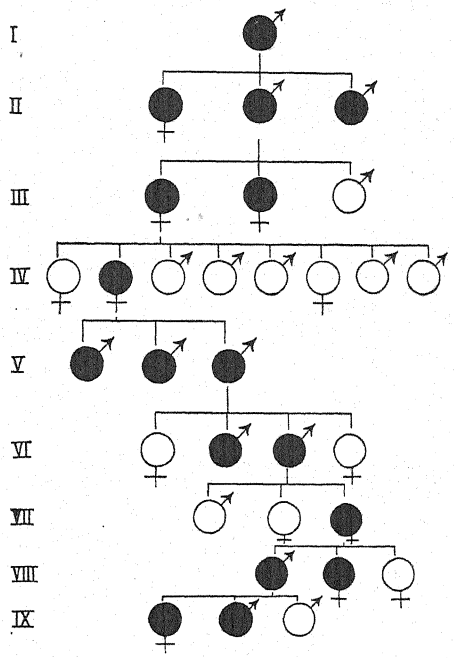
HIRSCHSPRUNG'S DISEASE. *After* GAUBLEN.

(Congenital Hypertrophy and Dilatation of Lower Part of Colon.)



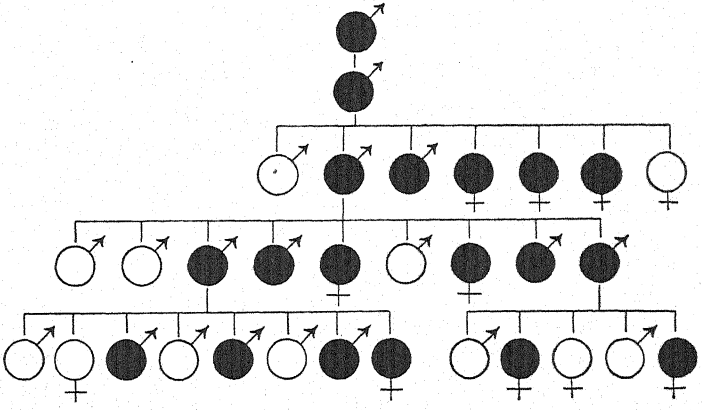
Dominant. All affected persons are heterozygous.

HEMERALOPIA (NIGHT-BLINDNESS).
After NETTLESHIP, abbreviated.



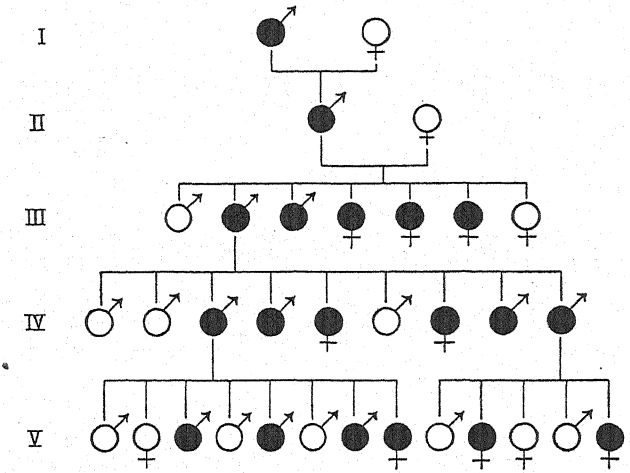
Dominant. All affected persons are heterozygous.

HYPOTRICHOSIS. *After* LINZENMEIER, abbreviated.



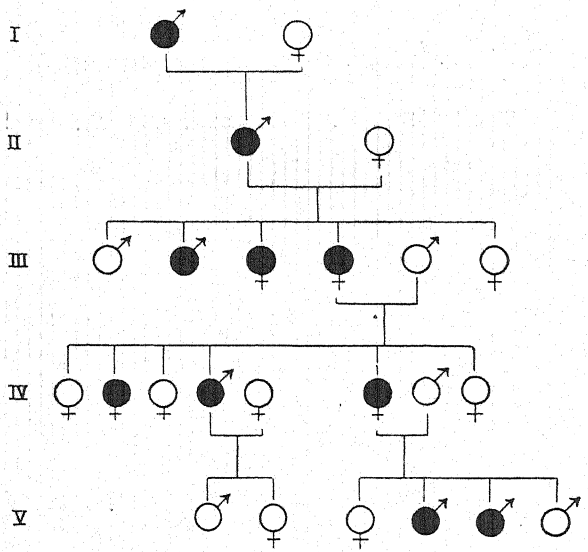
Dominant. All affected persons are heterozygous.

HYPOTRICHOSIS CONGENITA. *After* LINZENMEIER, abbreviated.



Dominant. All affected individuals are heterozygous.

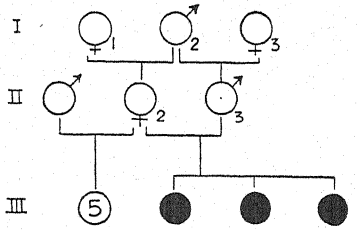
ICHTHYOSIS VULGARIS. *After* LEVEN.



Dominant. All affected individuals are heterozygous.

ICHTHYOSIS CONGENITA OR KERATOSIS UNIVERSALIS.

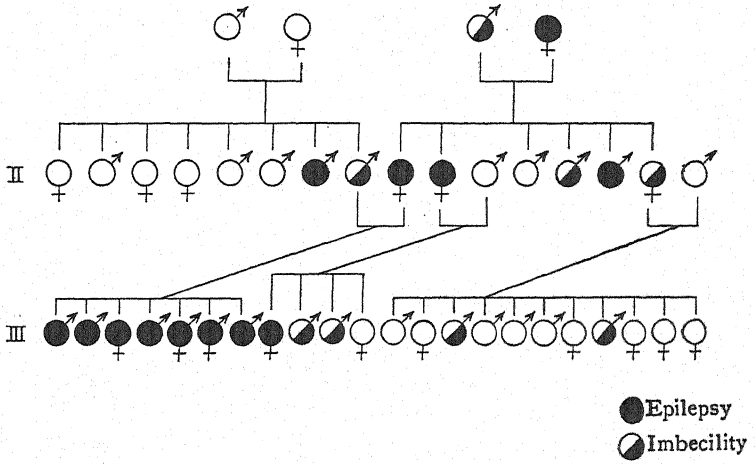
After CLAUS.



Recessive. Consanguinity. I, 2 is a carrier. II, 2 and 3 are carriers.

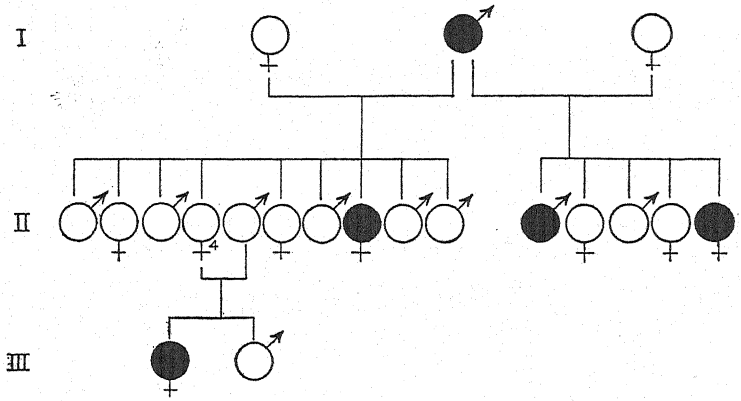
IMBECILITY, EPILEPSY, AND FEEBLE-MINDEDNESS.

After WEEK AND LAUGHLIN, abbreviated.



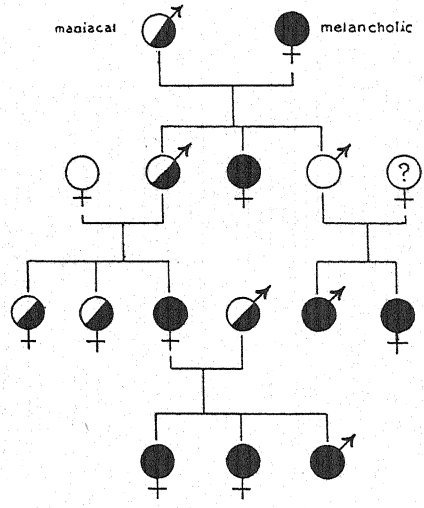
Epilepsy dominant (irregular).

LUXATIO COXÆ CONGENITA. *After* ROCH.



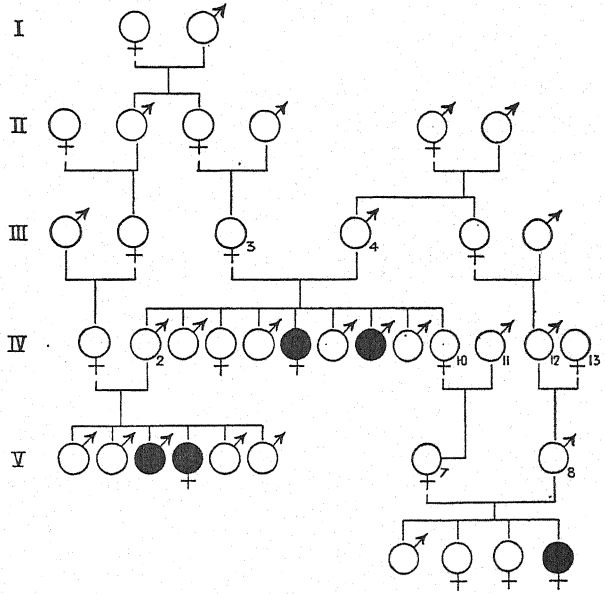
Dominant (irregular). All affected persons are heterozygous. II, 4 must carry the gene, although not exhibiting the character.

MANIAC DEPRESSIVE INSANITY. *After* HOFFMAN.



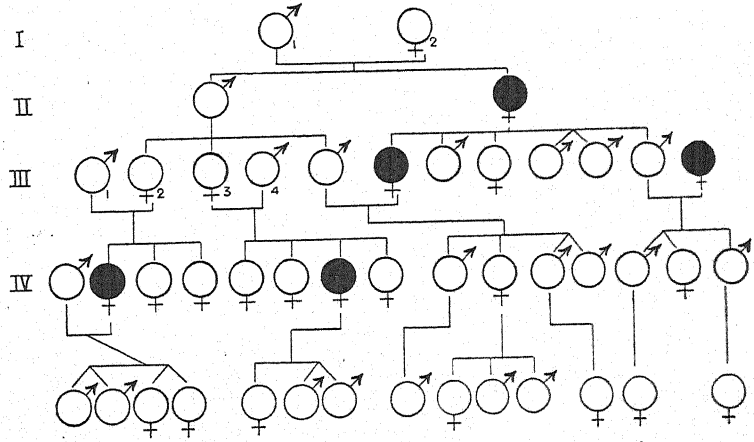
Dominant.

MICROMELIA (DWARFISM). *After* HANHART, abbreviated.



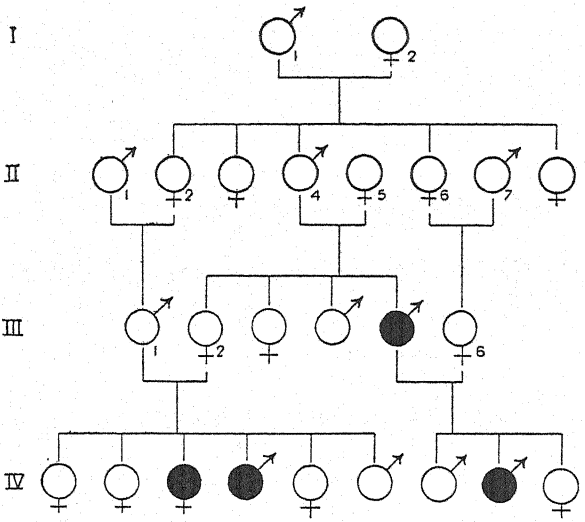
Recessive. Consanguinity. One member of each pair (at least) in I, II, and III is a carrier. III, 3 and 4 are both carriers. IV, 1 and 2 are carriers. IV, 10 and 11, 12 and 13, one member of each pair is a carrier. V, 7 and 8 are carriers.

MULTIPLE BIRTHS. *After* MEIROWSKY.



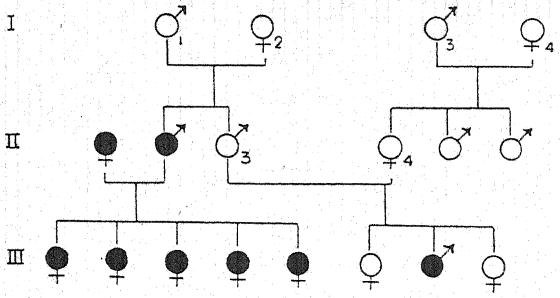
Recessive. I, both are carriers. III, 1, 2, 3, 4 are carriers.

MUSCULAR DYSTROPHY. *After* WEITZ.



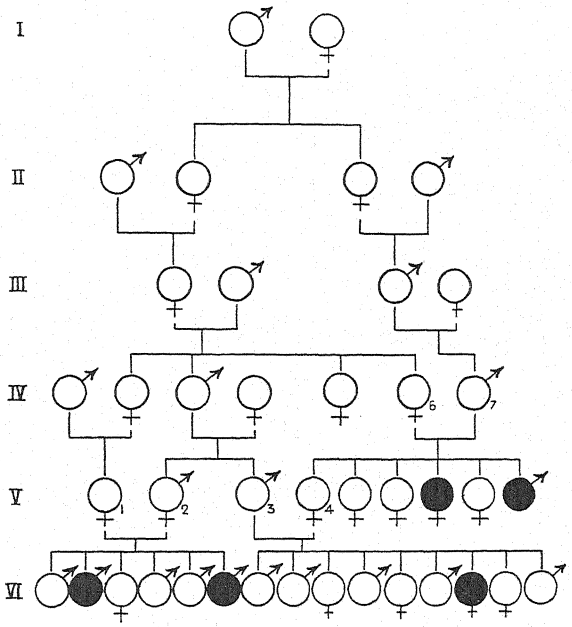
Recessive. Consanguinity. I, 1 and 2; II, 1 and 2, 6 and 7, one member of each pair (at least) is a carrier. II, 4 and 5; III, 2 and 6, are carriers.

MYOPIA. *After* CLAUSEN.



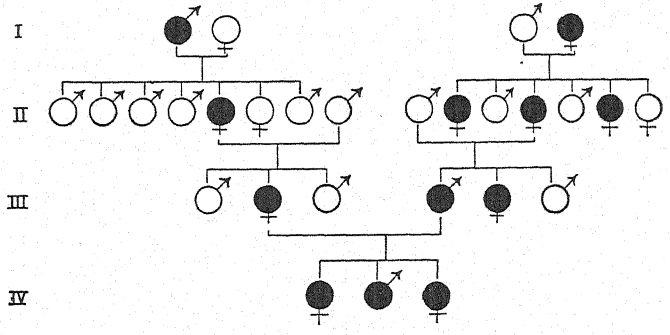
Recessive. I, 1 and 2, carriers; 3 and/or 4, carriers. II, 3 and 4, carriers.

MYOCLONUS EPILEPSY. *After* LUNDBORG, abbreviated.



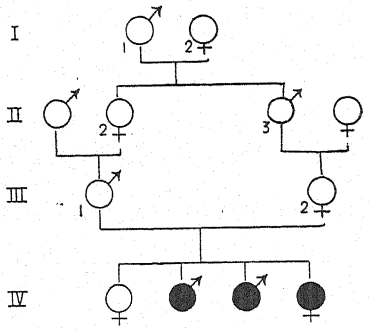
Recessive. I, II, III, IV, one member of each pair (at least) carriers. IV, 6 and 7, second cousins, carriers. V, 1 and 2, cousins; 3 and 4, cousins, carriers.

MYOPIA. *After* JABLONSKI.



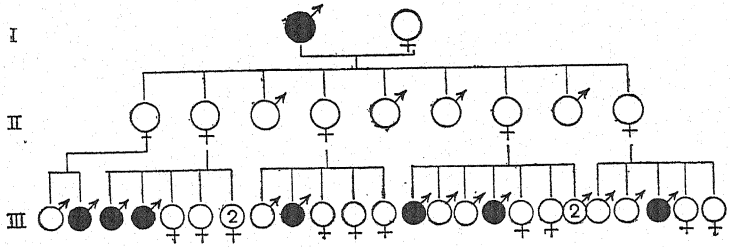
Dominant. I, II, III, all affected individuals heterozygous. IV, one or more may be homozygous.

NYCTALOPIA (DAY-BLINDNESS). *After* HESSBERG.



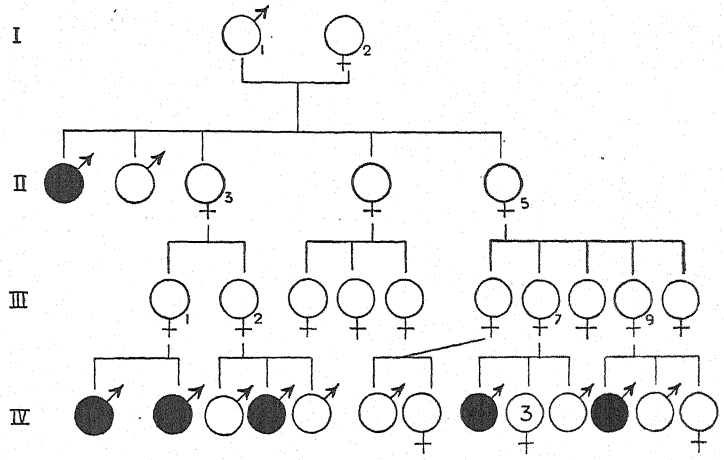
Recessive. Consanguinity. I, 1 and/or 2, carriers. II, 2 and 3, carriers. III, 1 and 2 are cousins and carriers. IV, 1, normal or a carrier.

NEURAL PROGRESSIVE MUSCULAR DYSTROPHY. *After* HERRINGHAM.



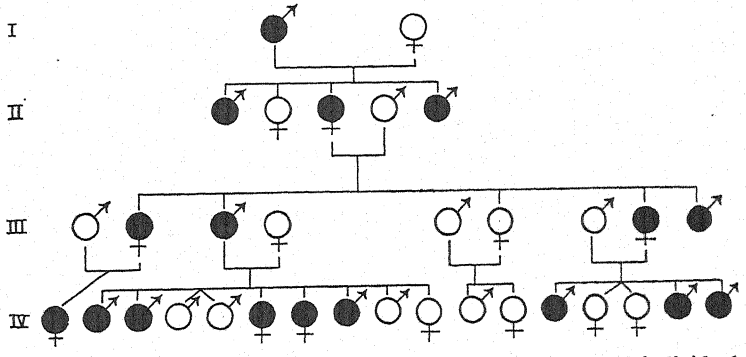
Recessive. Sex-linked. II, all females are carriers.

OPTIC NEURITIS. *After* HENSEN.



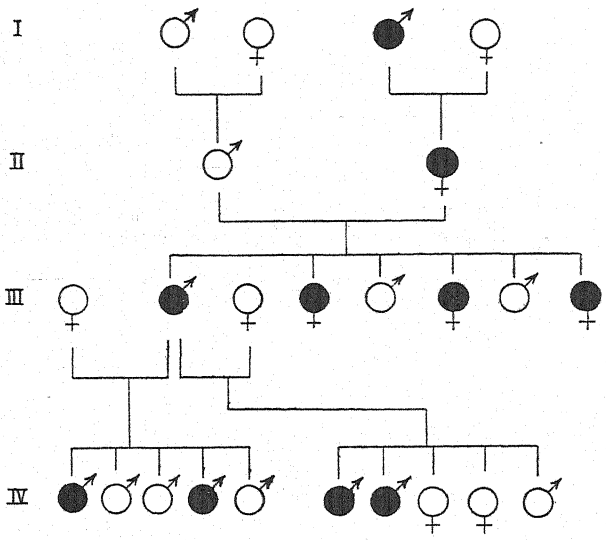
Recessive. Sex-linked. Carriers—I, 2; II, 3 and 5; III, 1, 2, 7, 9.

POLYDACTYLY. *After* SVERDRUP, abbreviated.



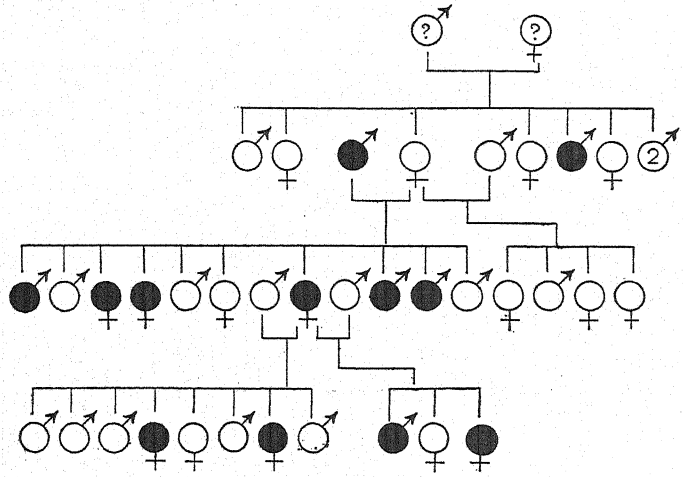
Dominant. Variable in degree of expression. All affected individuals are heterozygous.

PROGRESSIVE MUSCULAR DYSTROPHY.
After KEHRER.



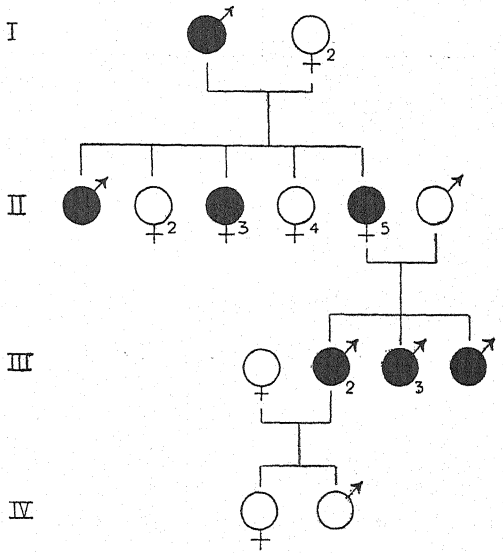
Dominant. All affected individuals are heterozygous.

RACHITIS. *After* ZEISCH.



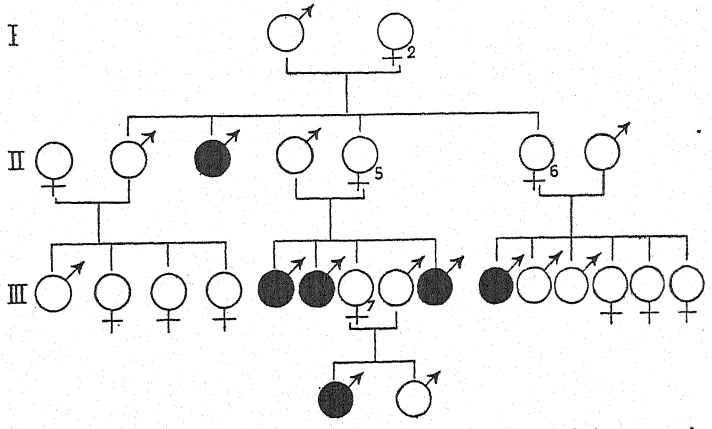
Multifactor, probably dominant. All affected individuals are heterozygous.

RED-GREEN BLINDNESS. *After* NAGEL.



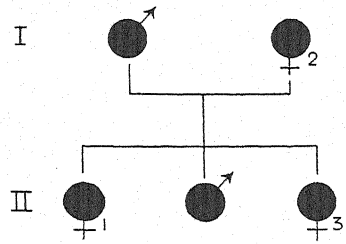
Recessive. Sex-linked. I, 2; II, 2 and 4; III, 1, are carriers. II, 3 and 5, homozygous, therefore III, 2, 3, 4, all affected.

RED-GREEN BLINDNESS. *After* GROENOUW.



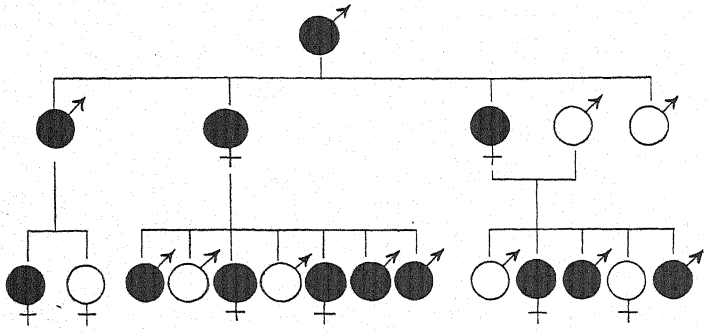
Recessive. Sex-linked. I, 2 is a carrier. II, 5 and 6 are carriers. III, 7 is a carrier.

RED-GREEN BLINDNESS. *After* VOGT.



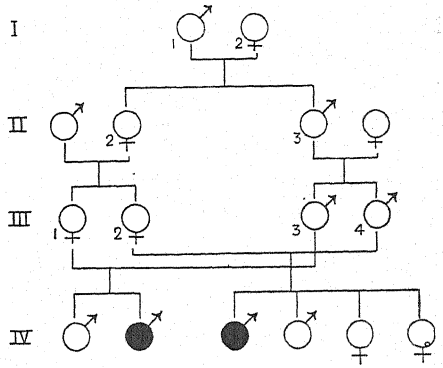
Recessive. Sex-linked. I, 2 must be homozygous, therefore II, all affected. (1 and 3 homozygous.)

DOMINANT RETINITIS PIGMENTOSA.
After NETTLESHIP, abbreviated.



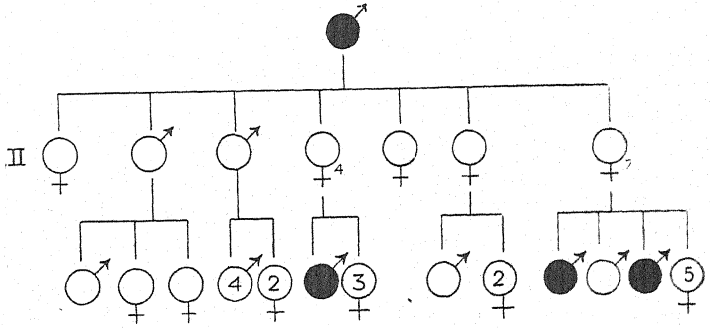
All affected persons are heterozygous.

RECESSIVE RETINITIS PIGMENTOSA. *After* BOEHM.



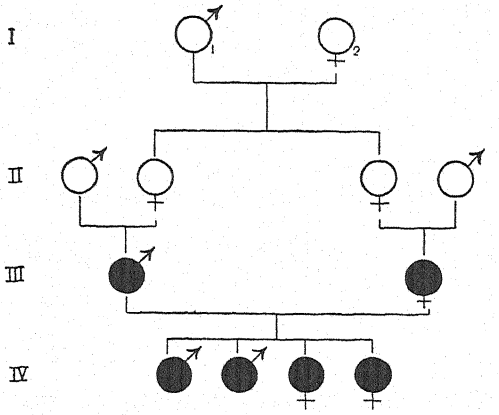
Recessive. Consanguinity. I, 1 and/or 2 are carriers. II, 2 and 3, carriers. III, 1, 2, 3, 4, carriers.

RETINITIS PIGMENTOSA. *After* NETTLESHIP.



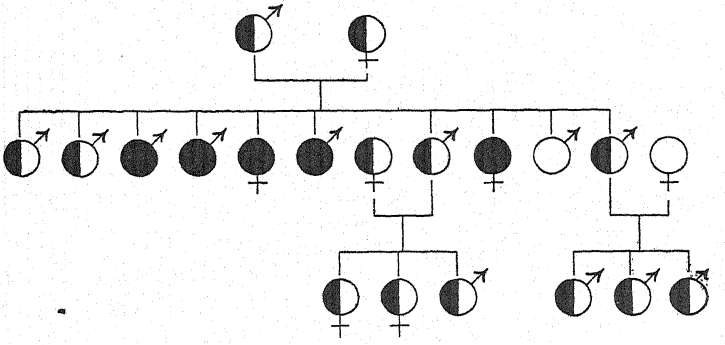
Recessive. Sex-linked. II, 4, 7, carriers.

SCARLATINAL NEPHRITIS. *After* LEUF.



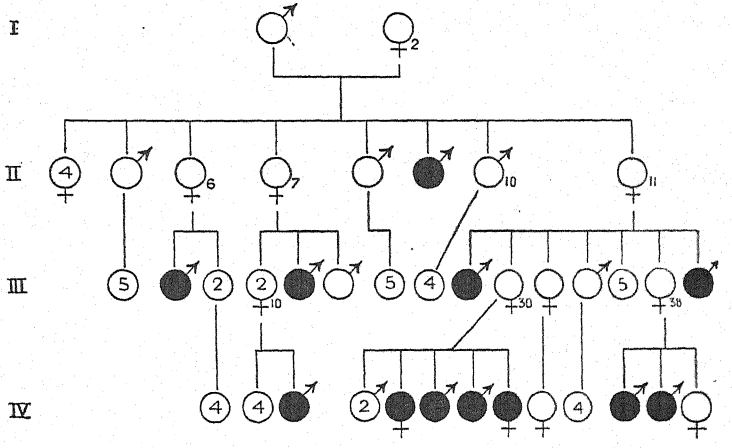
Recessive. Consanguinity. I, 1 and/or 2, carriers. II, all carriers.

SCHIZOPHRENIA (DEMENTIA PRÆCOX) AND SCHIZOID PSYCHOPATHIA. *After* HANHART, abbreviated.



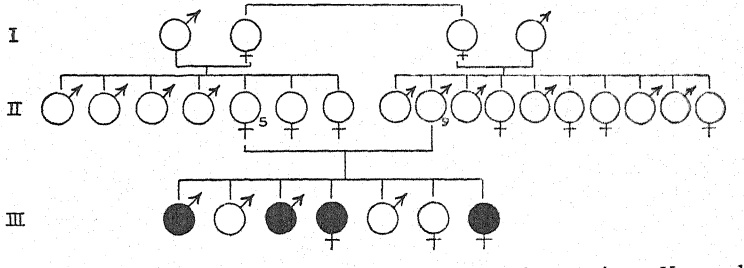
Recessive. Multifactor.

SPASTIC PARAPLEGIA (PELIZÆUS-MERZBACHER'S DISEASE).
After MERZBACHER.



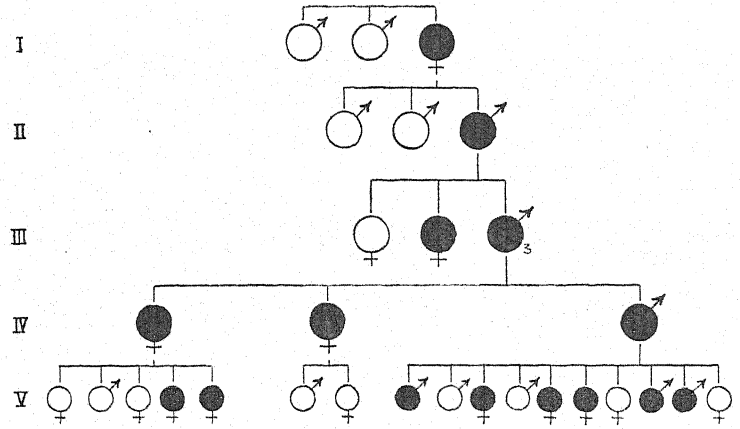
Confined to one family. Recessive. Sex-linked. I, 2 is a carrier. II, 6 and 7, carriers. III, 10, 30, 38, carriers.

SPASTIC PARAPLEGIA. *After* DAVIDENKO.



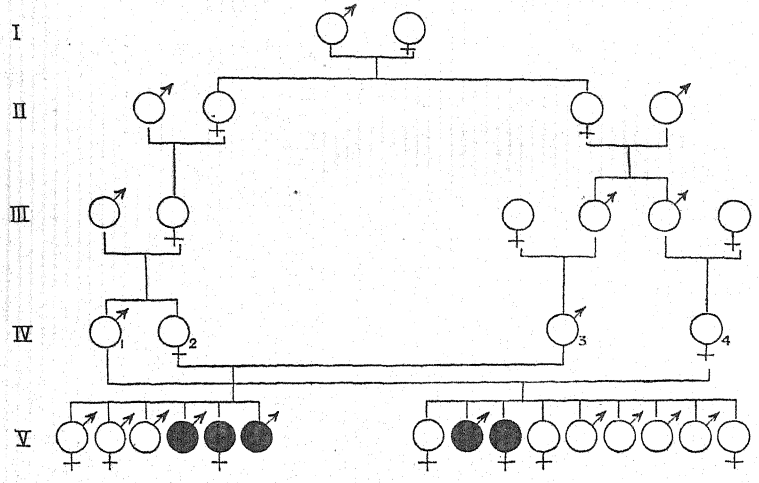
Recessive. I, one member of each pair (at least) is a carrier. II, 5 and 9, carriers.

SPASTIC SPINAL PARALYSIS. *After* BREMER, abbreviated.



Dominant. III, 3 possibly homozygous, probably heterozygous. All other individuals (affected) are heterozygous.

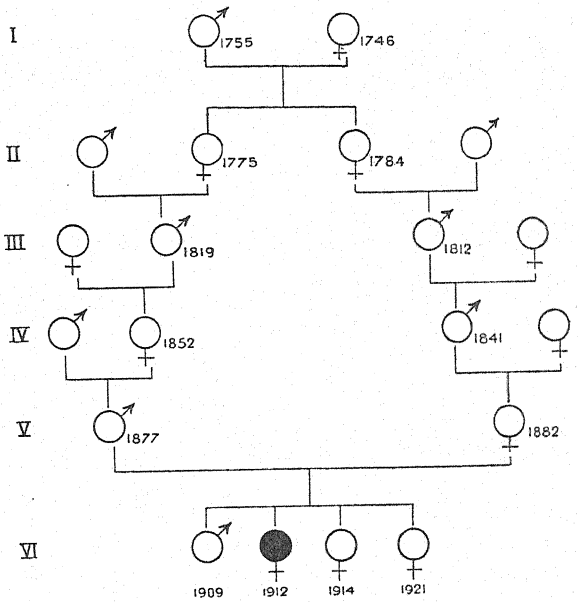
HEREDITARY SPINAL ATAXIA (FRIEDREICH'S ATAXIA).
After HANHART, abbreviated.



Recessive. One member of each pair (at least) in I, II, III must be carriers. IV, all are carriers.

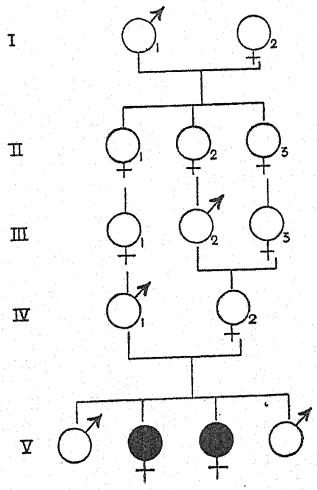
HEREDITARY SPINAL ATAXIA (FRIEDREICH'S ATAXIA).

After HANHART.



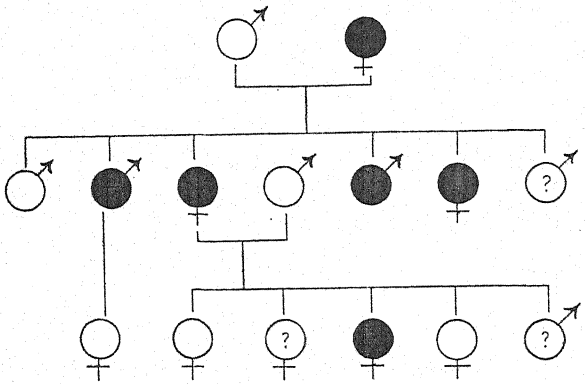
Recessive. One member of each pair (at least) in I, II, III, IV, must be carrier. V, both are carriers. Dates show year of birth.

SPASTIC PARAPLEGIA (SPINAL PARALYSIS). *After* ERB.



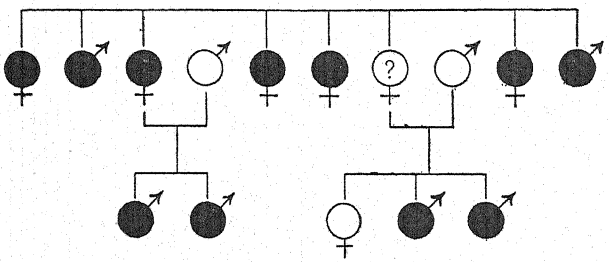
Recessive. Consanguinity. I, 1 and/or 2, carriers. II, 1, 2, and/or 3, carriers. III, 1, 2, and/or 3, carriers. IV, 1 and 2, carriers.

SUICIDE. *After* BREMER, abbreviated.



Dominant.

VALVULAR DISEASE OF THE HEART.
After STREBEL, abbreviated.



Dominant. Sex-linked.

INDEX

Biological Monographs and Manuals

General Editors:

F. A. E. CREW, Edinburgh.

E. WARD CUTLER, Rothamsted.

Medium 8vo. Cloth.

THE PIGMENTARY EFFECTOR SYSTEM. A Review of the Physiology of Colour Response. By LANCELOT T. HOGBEN, M.A. (Cantab.), D.Sc. (Lond.), Professor of Physiology, South African College, Cape Town. 164 pp. *net* £0 10 6

THE ERYTHROCYTE AND THE ACTION OF SIMPLE HÆMOLYSINS, by ERIC PONDER, Lecturer in Physiology in the University of Edinburgh. 204 pp. *net* £0 12 6

ANIMAL GENETICS. An Introduction to the Science of Animal Breeding. By F. A. E. CREW, M.D., D.Sc., Ph.D., F.R.S.E., Lecturer in Genetics in the University of Edinburgh, and Director of the Animal Breeding Research Department. With Coloured Plate, 66 Text-Figures, and Bibliography of 1500 References. 440 pp. *net* £0 15 0

STATISTICAL METHODS FOR RESEARCH WORKERS, by R. A. FISHER, M.A., Chief Statistician, Rothamsted Experimental Station. 252 pp. *net* £0 15 0

REPRODUCTION IN THE RABBIT, by JOHN HAMMOND, M.A. (Cantab.), School of Agriculture, Cambridge. With Foreword and Chapter on the Formation of the Corpus Luteum by F. H. A. Marshall, F.R.S. With 20 full-page Illustrations. 236 pp. *net* £0 15 0

THE COMPARATIVE ANATOMY, HISTOLOGY, AND DEVELOPMENT OF THE PITUITARY BODY, by G. R. de BEER, M.A., B.Sc., F.L.S., Jenkinson Memorial Lecturer in Comparative and Experimental Embryology in the University of Oxford. With 11 Plates (1 coloured) and 118 Text-Figures. 128 pp. *net* £0 12 6

THE COMPOSITION AND DISTRIBUTION OF THE PROTOZOAN FAUNA OF THE SOIL, by R. SANDON, M.A., General Microbiology Department, Rothamsted Experimental Station. With 6 full-page Plates and 3 Folding Charts. 256 pp. *net* £0 15 0

THE SPECIES PROBLEM, by G. C. ROBSON, M.A., Assistant Keeper, Department of Zoology, British Museum. 290 pp.

OLIVER AND BOYD

EDINBURGH: TWEEDDALE COURT

LONDON: 33 PATERNOSTER ROW, E.C.